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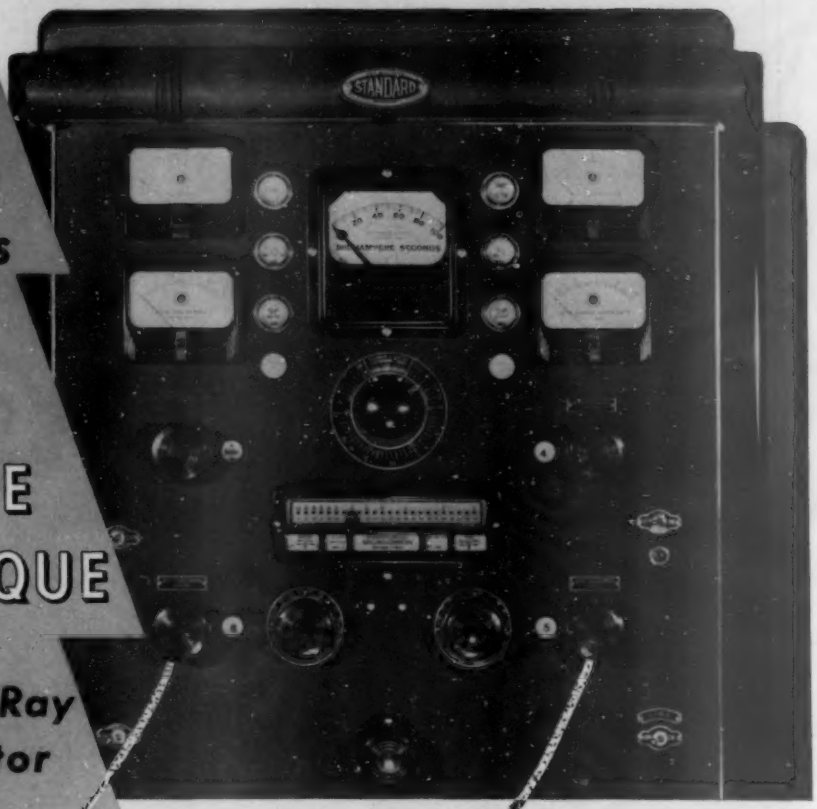

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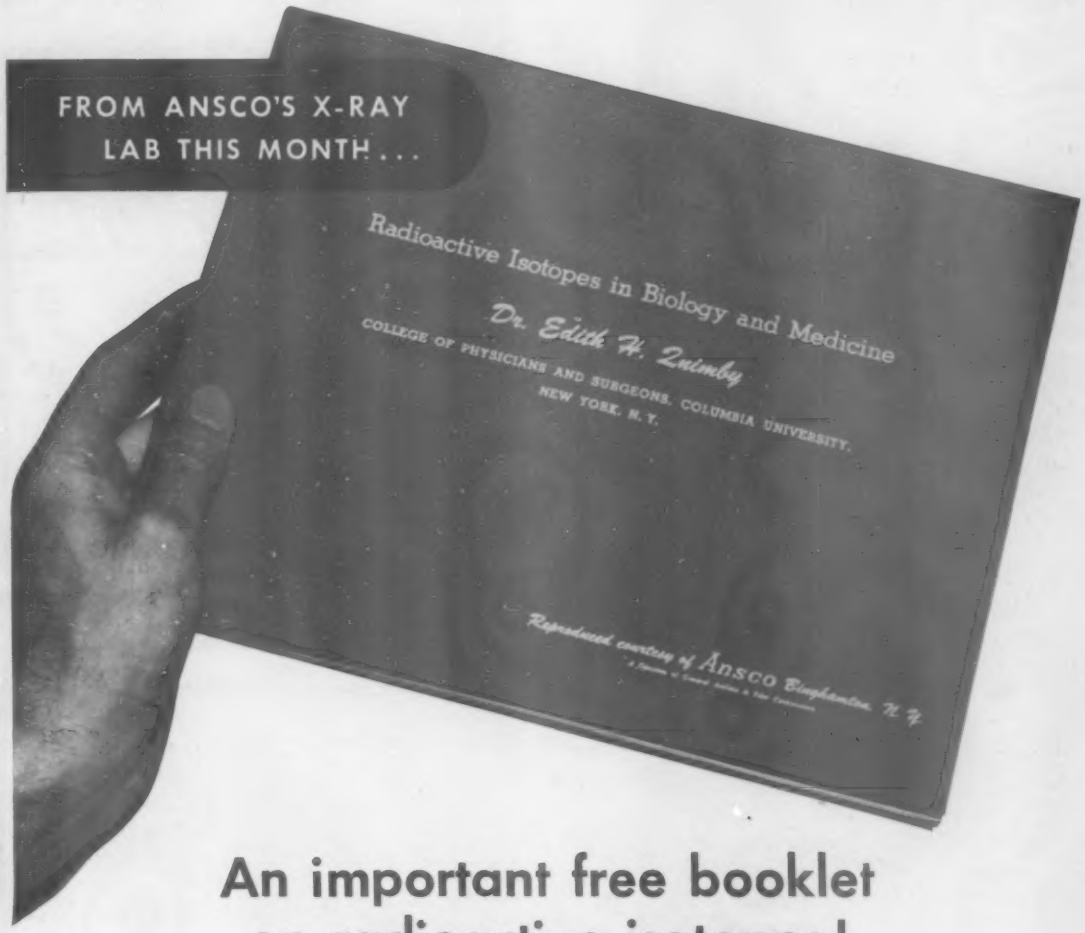
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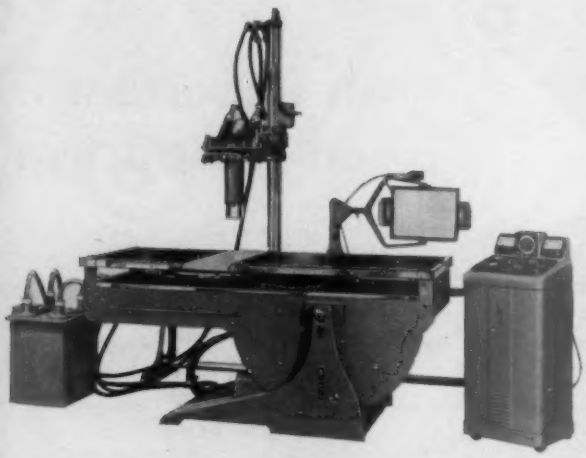

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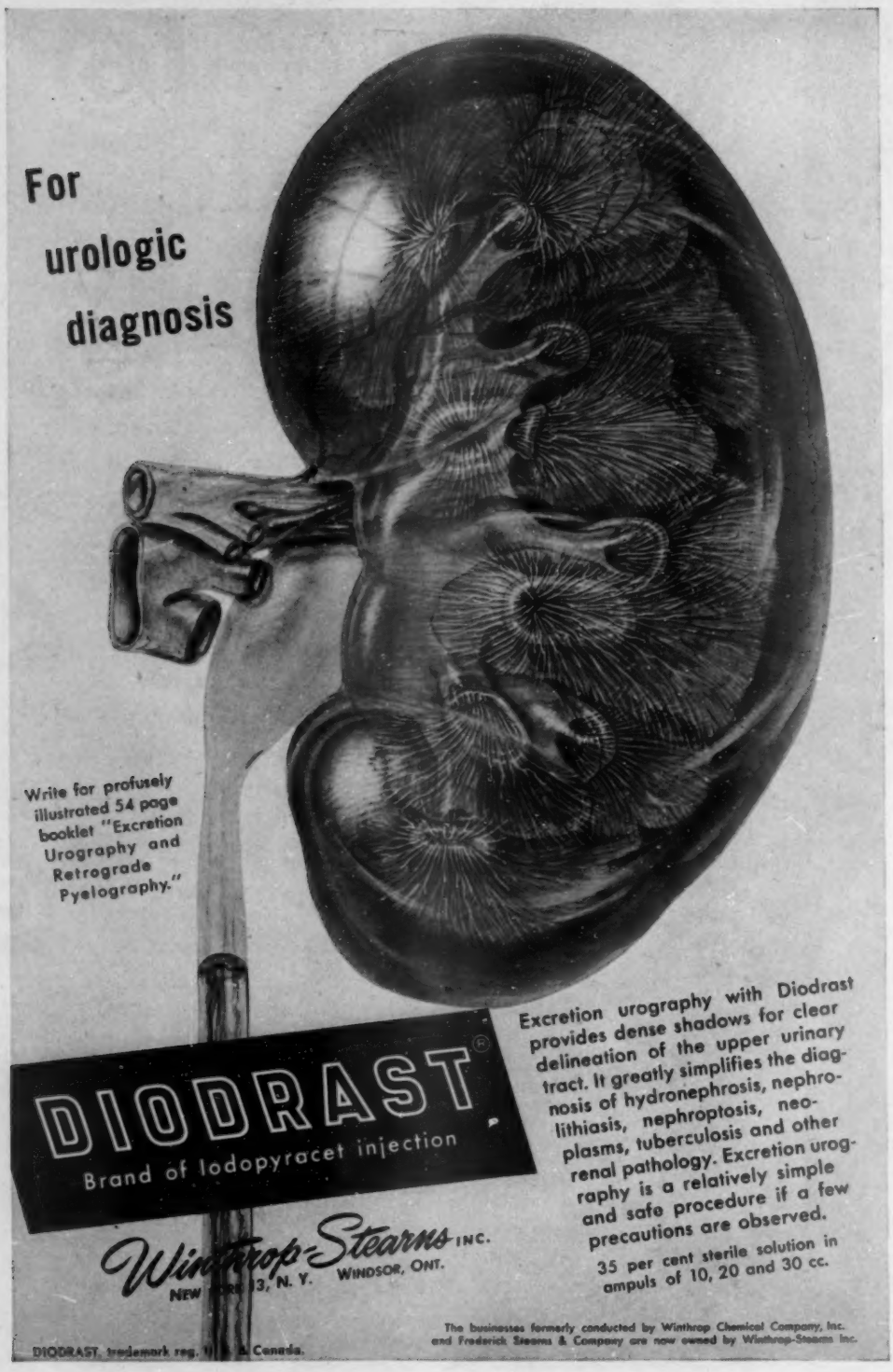
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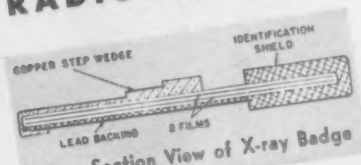

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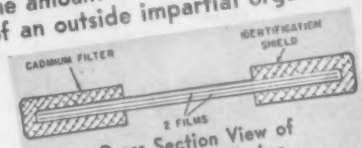

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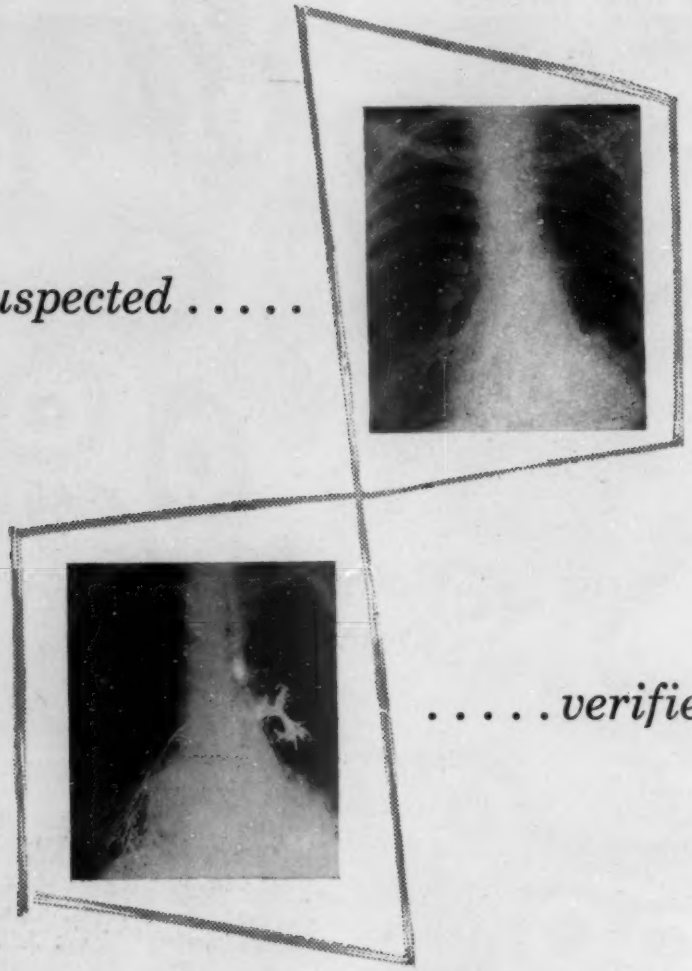

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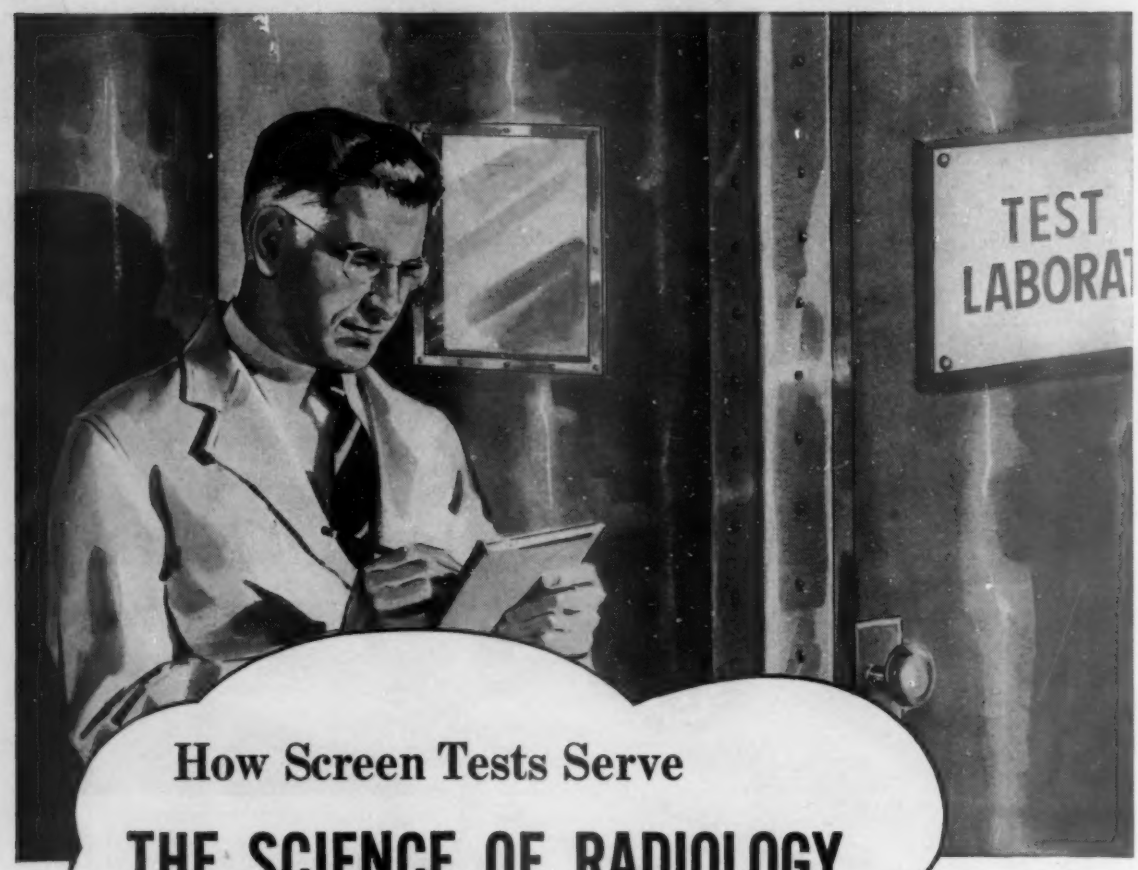

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TECHNIQUES FOR APPLICATION OF THE BETATRON TO MEDICAL THERAPY*†

WITH REPORT OF ONE CASE

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THIS paper is the account of an attempt to save a patient with glioblastoma by means of high energy roentgen rays from the betatron. The attempt was unsuccessful; the patient died. As a rule, a single therapeutic trial does not warrant a long write-up, especially if it is unsuccessful. We feel that in the present case an exception is justified. This was—as far as we know—the first patient to be treated with 20 million volt roentgen rays and with the betatron. The preparation for and the execution of this one course of irradiations involved a good deal of work in physics, as well as technical developments and clinical observations. The results may be of some value to the groups which are planning to investigate the clinical applications of the betatron.

The 22 mev. betatron of the University of Illinois, at Urbana, is an instrument dedicated primarily to physical research

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and development. In addition, the instrument has been used to explore some possible applications. One of these is the applicability of the betatron in cancer therapy. Some useful techniques had been developed.* At this state, we became interested in a patient who was suffering from a malignant brain tumor. He had been operated on and had been given a course of conventional radiotherapy without success. It seemed that the man had a small but not entirely negligible chance of cure if treated with the betatron. The moral issue was simple. We could let the patient die without disturbing him further, or he could be given a last chance. This could be done without much inconvenience either to him or to his family. There was little doubt as to which decision to make. As there was no other betatron available for clinical work at the time, it was proposed to use the 22 mev. machine at Urbana. The University authorities cleared the machine for use in this one case, and the staff of the Carle Hospital Clinic accepted the medical responsibility.

The task at hand was to coordinate miscellaneous relevant information and perform additional tests until one coherent method developed out of the various details. This took one week of rather concentrated work. Some components of this method have been the object of a preliminary publication in this JOURNAL,[1] and will be more fully expounded in this paper. Needless to say, our method is far from perfect. It is, however, an integrated solution which considers every major technical problem arising in radiation therapy, though in a very sketchy way. The method used here is a framework, sparse but coherent, which we hope will serve as a stimulus for the development of clinical methods. Our own group will continue the investigation of various problems which refer to cancer therapy. No further clinical work is planned at Urbana.

I. APPRAISAL OF RISKS OF HIGH ENERGY ROENTGEN RAYS

Before any new agent is introduced into clinical therapy, it is important to check any inherent dangers. The first problem to be investigated in the case of high energy roentgen rays is that of the possibility of specific, unexpected biological effects. Stone[12] has warned very earnestly against the use of high energy rays without previous exhaustive biological tests. We agree that the inherent dangers of high energy rays should by no means be taken lightly. However, Stone's warning is based on his experience with heavy particles, namely neutrons. We propose to show that, for physical and radiobiological reasons, unexpected effects are much less likely to occur with high energy roentgen rays than with heavy particles. The standards of our therapeutic experience are the 200 kv. beam, and the γ-rays of radium. The ionization tracks produced in tissue by these two types of radiation differ somewhat, the electron tracks produced by γ-rays have a lower specific ionization than those produced by 200 kv. rays. The tracks in a high energy roentgen-ray beam have a specific ionization slightly higher than those in the γ-ray beam. The difference is so small that, if one were to examine a number of random track segments of the length of a few cells, he would hardly be able to distinguish the γ-rays of radium from the 20 million volt roentgen rays. As a cell does not "see" more than a short segment of a track, it is difficult to see how it could distinguish the two. On the other hand, the densely ionized tracks of heavy particles are very easily differentiated from the thinly ionized electron tracks due to roentgen rays.

The elementary biological reactions in-

* We knew how to get a roentgen-ray beam free of electrons (D.W.K.); we had some experience in dosimetry, with ionimetric methods (D.W.K., H.W.K., P. Morrison,[7] L.S.S.), photographic methods (G.D.A.), induced radioactivity (A.O.H., J.S.L.), and bioassay (M. Baer, H. B. Chase, R. K. Clark, E.F.L., W. M. Luce, L.S.S., H.Q.); a collimator had been developed (D.W.K., H.W.K., E.F.L., L.H.L., H.Q.); the principles of filtering (S.M.D.) and the feasibility of a compensating filter were known (L.S.S.); problems of shielding had been studied (G.D.A., A.O.H., H.W.K.); a number of depth-dose distribution measurements had been taken (E.F.I., H.Q.).

duced are the same for all ionizing radiations. The difference in specific ionization finds an expression, however, in the dose-response relation. In general, there are two groups of reactions. In one type, roentgen rays are more effective than heavy particles, and in the other, they are less effective. The latter group seems to be the more important one as far as clinical effects are concerned. For various test reactions of this second class, the X/N ratios (ratios of doses of roentgen rays to neutrons, needed to produce the same biological effect) which are given in the literature[8] vary widely. Some of the variation might be due to differences in the measurement of doses. But, even as a most conservative estimate, the range of X/N ratios is certainly not less than 1 to 4. Large differences occur even between closely similar reactions, like the killing of mice by a single dose and by repeated doses.[4] If a heavy particle dose is effectively the same as a certain roentgen-ray dose with respect to one given reaction, it might be several times too high or low for some other reaction occurring in the same object. Therefore, if, in irradiating a highly complex organism, one matches roentgen-ray and neutron doses so as to have the same severity of some observed reaction, one cannot expect that all other reactions which may occur during or after treatment will be equally comparable in their severity (according to Stone's experiences, early and late reactions do not conform). Hence, while appropriate doses of heavy particles and roentgen rays can be found which result in equal severity for each single reaction, the total picture following a heavy particle irradiation, resulting from the relative intensity of a number of different reactions (and probably also from their interactions) might easily be distorted with respect to the picture obtained with 200 kv. rays.

The same effect occurs with high energy roentgen rays, but to a much lesser degree. The X/N ratios for one class of reactions vary over a range of at least 1 to 4. The X/γ ratios[8] for the same class of reactions vary from 1.3 to 2.0, which is a range of 1 to 1.5. Hence, when a roentgen and a γ-ray dose are matched to produce the same severity for one type of reaction, the discrepancy in severity on other, simultaneous reactions and, therefore, the distortion of the composite effect cannot be nearly as pronounced as for heavy particles. This is in agreement with the clinical experience that the effects of conventional roentgen rays and γ-rays of radium are nearly equal, if due allowance is made for the distribution of dosage in space and time. The physical effects of high energy roentgen rays within a given volume of cellular dimensions deviate only little from those of γ-rays, and the deviation is in the direction toward roentgen rays of conventional energy. The same should apply to biological effects. The results of the biological tests performed thus far agree very well with the physical findings (cf. section 2). No unexpected reactions have been found so far in a number of different living objects subjected to the 20 million volt beam of the betatron.

Another possible risk, of a different character, in high energy roentgen rays lies in the possibility of delivering high doses to sizeable regions in the depth. This situation might conceivably lead to toxic phenomena different from those encountered in conventional therapy. It will be necessary to do some animal experimentation in this direction.

Besides keeping in mind the two above-mentioned risks, which may or may not exist, one must avoid certain mistakes when using the betatron in therapy. Some of these will be mentioned briefly.

If a thimble chamber is placed in the beam without an additional surrounding wall (cf. section 3), the doses read will be much lower than the tissue doses. Such a practice would lead to internal burns.

The skin reaction on the entrance field is by no means a guide for judging the tolerance dose in the depth. The dose at the entrance field is small. The dose at the exit field is usually larger, but the dose in the

depth is highest (cf. section 3).

Failure to remove electrons from the beam greatly reduces the efficiency of the betatron beam (section 6). The electrons will spoil the transition effect due to the roentgen rays. Equally, roentgen rays would spoil the range effect of the electron beam if it were used in therapy.*

rely on the stopping power of tissue to shorten the irradiated region.

Precise alignment of the patient with the beam is more critical at high than at conventional energies, due to the negligible amount of lateral scattering in the former.

Thus, there are obvious risks which arise if a betatron is not used with great care.

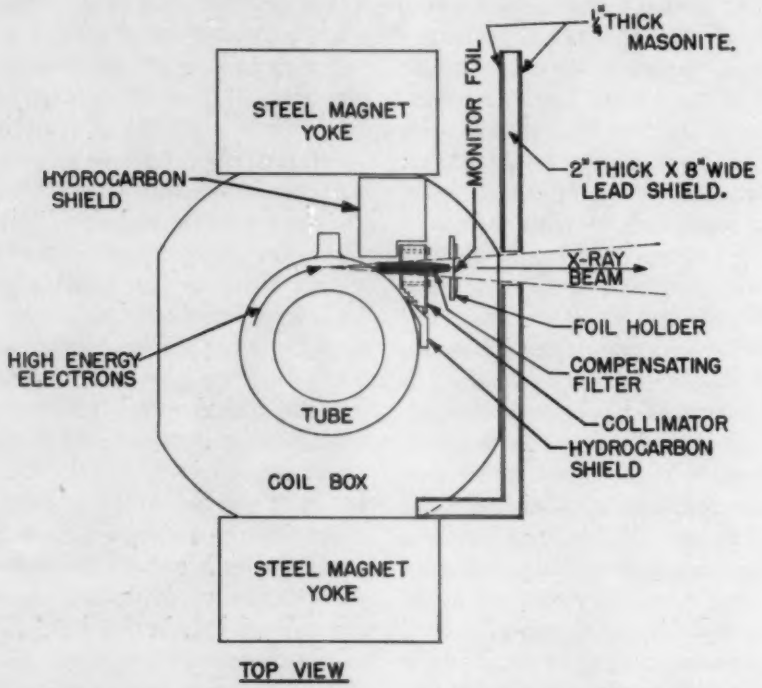


Fig. 1. Schematic top view of the 22 million volt betatron, showing arrangement of auxiliary instruments: collimator, electron and roentgen-ray shields, compensating filter, monitor foil. (Reproduced from Adams, G. D., *et al.*[1])

The whole depth between entrance and exit portal is likely to receive sizeable doses. One cannot, as at conventional energies, There may be other risks, which must be investigated by radiobiological research and, lastly, by clinical experience. Some,

* Since this paper was written, a paper by Charlton and Breed was published in this Journal, August, 1948. This paper contains a number of depth-dose distributions for uncollimated beams. Among the distributions shown are some for 20 million volt roentgen rays which indicate that the peak ionization occurs at a depth of about 1.5 cm. below the surface of a presdwood phantom, the surface being 132 cm. from the target. This is a definite disagreement with the work of Koch, Kerst, and Morrison which gave the peak ionization depth at about 3.5 cm. for a target-surface distance of 45 cm. If the data of Koch, Kerst and Morrison had been converted to a target-surface distance of 132 cm. (as they were not), the peak found would correspond to that obtained by Charlton and Breed at about 40 million volts.

The curves of Charlton and Breed are typical of those observed with the roentgen-ray beam heavily contaminated with concomitant electrons. If the electrons had been removed from the roentgen-ray beam, the ionization peak would have been deeper and the decline thereafter more gradual. This is clearly illustrated in their Figure 18. As a matter of fact, the 20 mev. depth-dose curve shown in their Figure 12, although it does show a transition effect, nevertheless declines more rapidly than the depth-dose curve for 1 million volt roentgen rays. This illustrates clearly the disastrous effect of electrons which contaminate the roentgen-ray beam. Means for removing these electrons are well known, and commercial betatrons which have been in the field for years were equipped with these means from the start. The workers in this laboratory have taken rather elaborate precautions to eliminate these electrons, as pointed out in the present paper. Such precautions are absolutely necessary in order to study the behavior of a pure roentgen-ray beam.

but by no means enough, of the radiobiological work has been done. Still, we feel that we now know enough about the betatron to warrant its use in selected clinical cases. The risk involved seems smaller than the opposite risk which is incurred if the betatron is withheld for a long period of time from patients who might benefit by its use.

tenuates the primary beam somewhat, so that the dose measured is not the true roentgen-ray flux.

There is, on the other hand, no difficulty in measuring tissue doses at high energy. A Victoreen dosimeter, introduced into a suitable phantom, yields a reading which is proportional to the tissue dose. The readings are claimed by the manufacturer to be

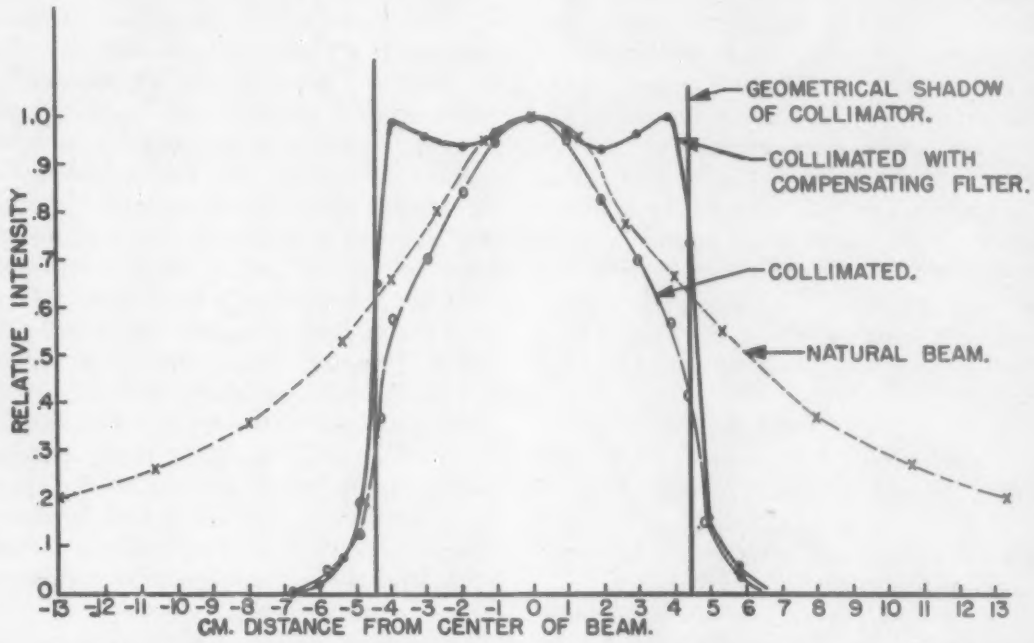


FIG. 2. Distribution of intensity across the beam. (Note: the cross section through the natural beam has been taken under conditions slightly different from those from the two collimated beams.) (Reproduced from Adams, G. D., *et al.*[1])

2. DOSIMETRY

The measurement of doses of high energy roentgen rays with a standard open air chamber is impractical because the secondaries travel so far that a chamber of enormous dimensions would be needed. Measurements with thimble chamber type instruments are feasible. However, the walls surrounding the thimble must be sufficiently thick to permit equilibrium between the primary beam and the secondary electrons to be established. Using material of a density similar to that of tissue, the wall thickness required at 20 million volts is about 10 cm. A wall of this thickness at-

independent of energy up to 1 mev. No claim for absoluteness in the multimillion volt region is made; and indeed, evidence has been obtained indicating that the units read are not absolute roentgens at 20 mev. One indication of this is the fact that thimble chambers of different capacities give normalized readings at 20 million volts which are different from those obtained at 200 kv. Tests were made which showed that any differences in readings are not due to ionization produced in the metal stem of the dosimeter.

As far as clinical application is concerned, however, a definite meaning can be given

to the units read if the dosimeter is calibrated by bio-assay. The techniques of such bio-assays are sometimes tedious and delicate, but always straightforward. A dose-response relation is established between any biological reaction and doses measured, in a beam of conventional energy (200 kv.). Subsequently, the relation between the same reaction and doses as measured with the Victoreen dosimeter is obtained in the beam of the betatron, taking care that no factor except the quality of the rays is different in the two sets of experiments. The two curves obtained are compared, and it is ascertained whether or not they differ only in the units of the dose axis. If this is the case, then the ratio of the units is a parameter which permits one to convert betatron doses as read with the Victoreen dosimeter into doses of conventional rays which produce the same effect with respect to the given biological test reaction.

Strictly speaking, any such conversion factor applies only to the set of conditions for which it was obtained. It might be permissible, however, to extend it to closely related reactions and conditions. In order to obtain a broad basis for evaluation, reactions of a very diverse nature have been investigated. These include local and general reactions in mice, fruit flies, and beans (references 2, 9, 10, and unpublished material). In every case thus far examined, the conversion factor was close to 0.75. In other words, by multiplying the reading obtained with the 25 r Victoreen thimble in the betatron beam (thimbles of other capacities have other factors) by the factor 0.75, one obtains a dose measure which allows one to predict the biological effects in the light of experience with 200 kv. rays. The unit of this dose measure we call the r.e.b.a.—roentgen equivalent by bio-assay.

We disclaim any identity of the r.e.b.a. with the "biological roentgen" or the "rem." The r.e.b.a. is a much more modest unit, which makes no claim of universality and does nothing but reflect a certain amount of experience which has been gathered, and some extrapolation. One need not by any means expect to find exactly the same conversion factor for every reaction, but it seems that, for the present state of accuracy in clinical work, the unit is sufficiently precise (± 5 per cent).

For purposes of relative dosimetry, photographic film is often relied on. It has been established that, in Eastman Industrial X-Ray Film, Type A, the density above fog increases linearly with dose, at least over the practical range of densities (Fig. 5). This has been tested for energies between 10 and 20 million volts, the conditions of development having been carefully standardized. Therefore, ratios of densities are ratios of doses. We have established also that the dose-density relation remains the same at several points in a presdwood phantom, comprising a large range of distances both from the surface and from the center of the beam. Hence, it is not markedly influenced by such quality changes as occur when the beam traverses tissue-like material. One can conclude, then, that isodensity curves are isodose curves. The photographic film is a valuable tool for ascertaining depth dose distributions if the measurements are supported by ionimetric checks at selected points.

Another method of measuring roentgen-ray doses, especially during treatment with the betatron, is that of using a thin foil, placed perpendicular to the beam, in the fringing field of the betatron magnet. Under proper conditions, the radioactivity induced in the foil will be a measure of the dose delivered. Care must be taken to select a foil material with an appropriate half-life, and a threshold energy well below the peak energy of the roentgen rays. Also, this peak energy must be kept constant. The number of radioactive atoms, N, at a time τ after the end of the irradiation is given by

$$N = \frac{k}{\lambda}\,(1 - e^{-\lambda t})e^{-\lambda \tau}$$

(k = constant, λ = decay constant, t = time of irradiation). The radioactivity produced can be calibrated in terms of a Victoreen

thimble located in a presdwood model of the object to be irradiated.

To avoid variable screening effects due to the patient's body, it seems inescapable that the monitor used during treatment must be placed in the beam between target and patient. Means must therefore also be provided to remove the secondary electrons produced in it. A very satisfactory dosimeter for monitoring would be one which indicates the dosage rate continuously during irradiation, e.g. a flat ionization chamber, which would satisfy the limitations on electrons in the beam.

3. DEPTH DOSE DISTRIBUTION

The dominant process in the absorption in tissue of 20 million volt roentgen rays from the betatron is the Compton effect. Pair production occurs to a lesser degree, and atomic and nuclear photoeffects account for a fraction of a per cent of the total energy absorbed. The electrons and roentgen-ray secondaries produced in the Compton process are usually of high energy and travel almost entirely in the forward direction. The secondary electrons have considerable ranges (0.5 cm. per mev. in water) and their specific ionization is almost constant until the energy is reduced to a few hundred kilovolts.

These statements contain implicitly all the important characteristics of the depth dose distribution in high energy roentgen-ray beams. The first such characteristic is a transition effect. As the beam proceeds into tissue from air, the primary beam is attenuated, but electrons originate in every layer traversed. As these electrons have considerable range, the total electron flux is increased up to a certain depth beyond the surface. As the electron flux is by far the largest single factor responsible for the tissue dose, the latter will increase as the beam proceeds from the surface to a depth of a few centimeters (Fig. 3).

The increase in dose from the surface to a maximum was estimated to be about threefold in earlier measurements. According to the most recent measurements by W. V. Mayneord and J. H. Martin, it is about eightfold. The steepest gradient occurs near the surface; therefore, any measurements of surface doses are exceedingly sensitive to the thickness of the wall of the chamber. The peak of the tissue dose is broad and flat. With 20 million volt rays, the dose stays almost constant from 2 to 6 cm. depth. Beyond that, the tissue dose decreases slowly.

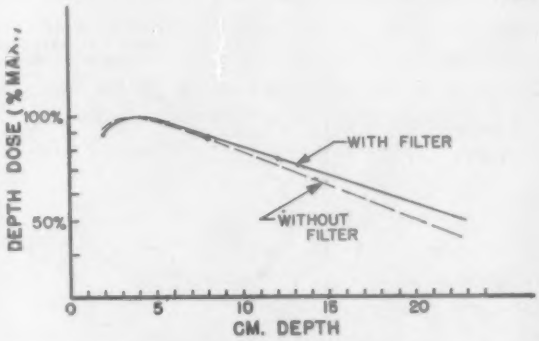


FIG. 3. Depth dose—center line. Water phantom at 100 cm. Circular beam, 11 cm. diameter. Thimble chamber measurement. (Reproduced from Adams, G. D., *et al.*[1])

The second depth dose characteristic is the great penetration of the beam. This fact is less striking than the transition effect but is far more important for clinical application.

The fact that the secondaries travel practically in the forward direction accounts for a third characteristic, that the amount of diffusion outside the geometrical edge of the beam is very small, and for a fourth characteristic, that field size is of little influence on the isodose curves. It follows that, if the dosage distribution perpendicular to the beam direction at one depth, as well as that along the central ray, is measured, then the complete three-dimensional distribution can be approximately calculated by applying to other rays appropriate factors determined from the measurement perpendicular to the beam.

Our experimental depth dose work was done with several phantoms. A water phantom was used in some cases. A presdwood

phantom with a flat thimble chamber had been used earlier.[7] The phantom used most extensively was one made of tempered presdwood sheets (density 1.12 gm/cc.), each $\frac{1}{8}$ inch thick. These sheets were stacked to make a cube, 40 cm. on a side, and set into a frame equipped with screws to press the sheets together. Presdwood plugs, $1\frac{1}{4}$ inches square and 9 inches deep, fit into holes provided at various depths from the surface of the phantom and at some extra-axial positions. They could be replaced by plugs drilled in such a way as to fit tightly over a Victoreen thimble. Victoreens in these positions were used for ionimetric checks on film data. Alternate presdwood pieces which accommodate small pieces of film in positions coinciding with centers of the Victoreen thimbles were employed to establish the independence of the dose-density relation from position in the phantom (cf. section 2). When it became clear that we could rely on photographic tests for relative dosage measurements, this method was used predominantly.

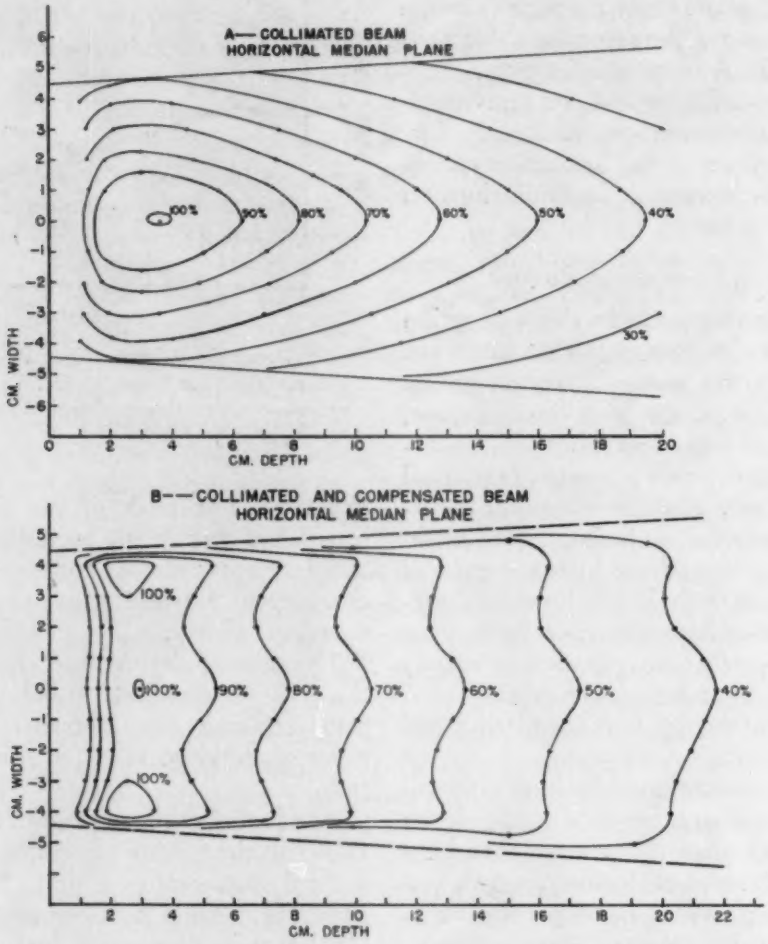


Fig. 4. Depth dose distributions. Presdwood phantom at 75 cm. Circular beam of 9 cm. diameter. Photographic measurements with thimble chamber spot checks. (Reproduced from Adams, G. D., *et al.*[2])

For such measurements, films in paper cassettes were placed between the presdwood laminations at various depths in a direction perpendicular to the beam or, in

some cases, parallel to the axis of the beam. Film densities were measured and the results expressed in depth doses with the help of the dose-density curve (Fig. 5).

Figure 4 shows an isodose curve obtained in a collimated beam. The dosage distribution for an uncollimated beam was published in an earlier paper.[10] The distribution in the collimated beam is the same up to the vicinity of the edge of the field, where the dosage gradient becomes very steep. Another set of curves shows the dosage distribution obtained with a compensating carbon filter (Fig. 7). This was the first filter designed and constructed by us, and, as the curves clearly show, does not flatten the field completely. Curves are given for incidence at 90°, 60°, and 30° angles with the phantom surface, achieved by rotation of the phantom about a vertical axis. The distributions in the horizontal plane are, of course, different in the three cases. However, in every case the isodose curves remain approximately parallel to the surface. Only one dose distribution in the vertical plane is shown, for this distribution is little, if at all, influenced by the angle of incidence. A depth dose distribution obtained by an improved filter is shown in Figure 4.

The presence of electrons in the roentgen-ray beam can be recognized by their effect on the depth dose characteristics. In a beam of electrons, the dose is roughly constant from the surface to a depth characteristic of the electron energy, and then falls off rapidly. Thus, electrons mixed with the roentgen rays will increase the dose in the first few centimeters below the surface without contributing to the depth dose.* This effect is brought out very well on films exposed parallel to the direction of the beam. On such films, the electrons concomitant with the roentgen-ray beam may appear as a dark band at the end toward the betatron. On depth dose curves, the effect of these electrons is to exaggerate the hump. Beyond the maximum the curves will show the definite break which is characteristic of the electron range. With thimble chambers, the presence of electrons can be demonstrated by not providing thick surrounding walls. The difference in readings obtained with and without a thick wall surrounding a thimble chamber gives an estimate of the relative proportions of roentgen rays and electrons. The curves published here have been obtained with a beam which was made practically free of electrons (cf. sections 4 and 6).

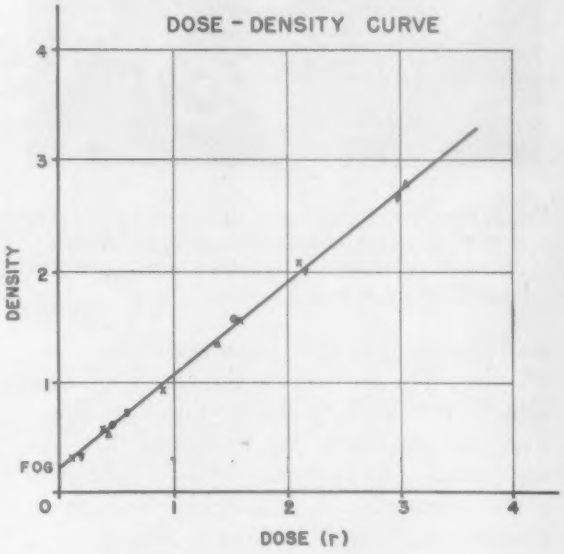


Fig. 5. Film density vs. dose. Eastman, Industrial "A," 20 mev. Dose in units read on the Victoreen ionometer. Each symbol indicates a different position in the phantom.

Conventionally, therapeutic tissue doses are expressed in percentages of the surface dose. This would not be practical in high energy beams because, as pointed out earlier, the measurement of the surface dose is exceedingly delicate and extremely sensitive to the wall thickness of the measuring instruments, and also the presence of nearby scattering objects. It seems reasonable to express all doses in percentage of the maximum dose. As can be seen from the figures, the dosage gradient in the region of the maximum is comparatively small; therefore, the measurement of the maximum dose is not very sensitive either to the

* For typical examples, see curves published in article by Charlton and Breed quoted in footnote on page 594.

Fig. 6. Presdwood phantom with several plugs drilled to fit tightly on Victoreen chambers, for ionimetric checks. Solid plugs are used for film tests. Several large films are in position.

wall thickness or to the exact position of the thimble. We use this maximum tissue dose also to check the output of the machine. For such purposes, the Victoreen thimbles are placed into cylinders of hard rubber or plastic materials of several centimeters diameter. Such measurements give a good approximation to the maximum tissue dose. When a Victoreen thimble is covered with a lead cylinder of $\frac{1}{8}$ inch thickness, we find that the readings obtained are consistently higher by about 75 per cent; this applies in air as well as behind 5 inches of wood.

4. COLLIMATOR

In therapy, one must be able to produce beams of various desired cross sections. With roentgen rays of conventional energy, a set of diaphragms and a few sheets of lead or lead rubber are all that is required for that purpose. With high energy roentgen rays, the technical problem is more complex.

The absorption coefficient of lead for roentgen rays produced by 20 mev. electrons is 0.44 cm.$^{-1}$ Thus about 5.25 cm. of lead is required to reduce the radiation intensity to 10 per cent, which is still much more than can be tolerated outside the geometrical beam. This means that quite a thick lead barrier must be used to confine the beam to the desired aperture. However, the lead need not surround the target on all sides, since the roentgen-ray beam emerging from the betatron has an intensity distribution which varies very markedly with direction. The maximum intensity is in the direction of the electrons striking the target. At an angle of 4° from the central ray the intensity is one-half, at 8° it is one-fourth of the maximum value and continues to decrease with increasing angle (Fig. 2). Consequently, the thickness of lead needed to reduce the intensity to a given fraction of the maximum intensity decreases with angle. A thick lead absorber

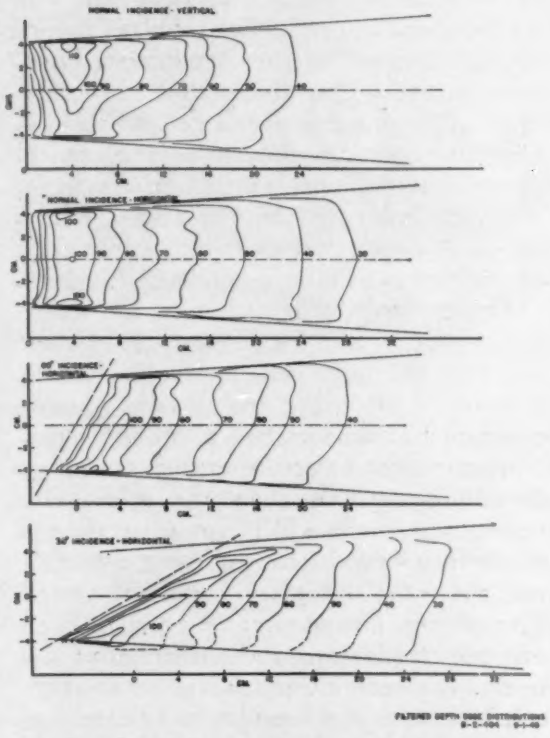


Fig. 7. Depth dose distributions. Presdwood phantom at 75 cm. target distance, photographic measurements with ionimetric checks. The beam is collimated, a compensating filter is used (the imperfect first model; compare Fig. 4 for the effect of a filter of better design). Angle of incidence: 90° in the vertical, 90°, 60°, and 30° in the horizontal plane.

is needed only for the central region of the beam.

In the process of absorption of roentgen rays in the collimator material, secondary electrons are produced. These electrons travel mostly in the forward direction, and would reach the patient together with the roentgen-ray beam. This would add considerably to the dose at and near the surface, and interfere with the valuable transition effect. These electrons must therefore be removed. This cannot be done by absorption in light weight material; a layer of several centimeters thickness would be needed, and that would again spoil the transition effect by moving the maximum dose toward the surface. The secondary electrons can best be removed by magnetic deflection. A convenient way of accomplishing this is to place the collimator between the coil boxes, in the magnetic field of the betatron. This automatically yields another advantage; moving the collimator into the proximity of the target reduces the bulk of the shield necessary to cover a given angle. On the other hand, lead is conducting and, when placed in a changing magnetic field, will give rise to disturbing eddy currents. By using thin insulated laminations, the eddy currents can be reduced to such an extent that they neither interfere with the nearby electron stream in the accelerating tube nor cause excessive heating of the metal.

Our collimator consists of a stack of 1/32 inch lead sheets, electrically insulated from each other by pieces of 0.010 inch fish paper. The total thickness of lead used is $2\frac{1}{2}$ inches. The laminations are held together by insulated brass bolts; $\frac{1}{8}$ inch brass plates are added in front and back for mechanical stability. The overall thickness of the collimator is about 3 inches. The details of the construction are shown in the diagram (Fig. 8) and its position in the betatron in Figure 1, and in the photograph (Fig. 9).

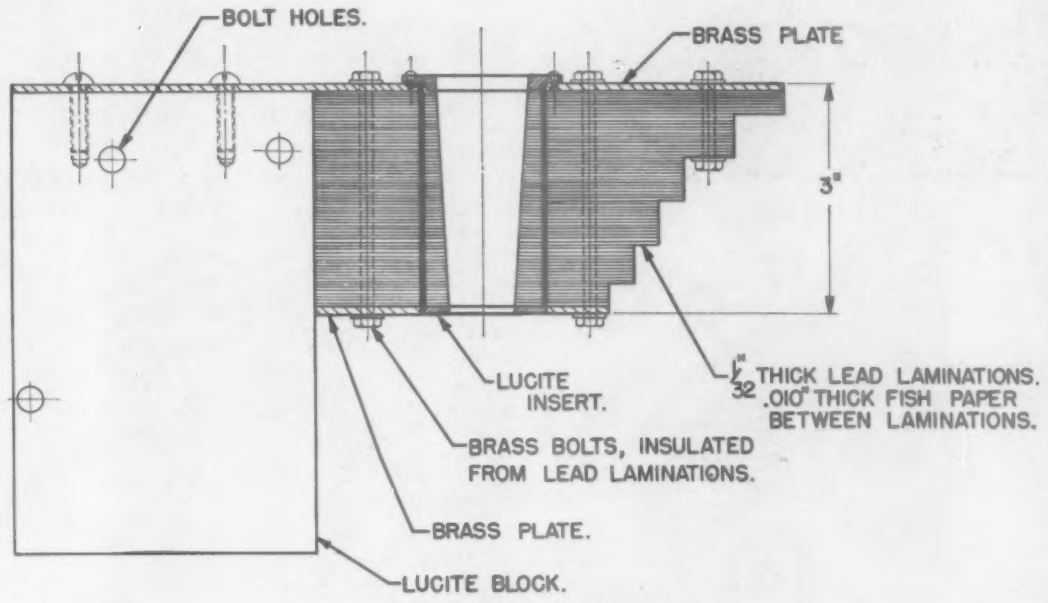


Fig. 8. Collimator construction.

For aligning the collimator, the target position is located, the direction of the roentgen-ray beam determined, and the center of the beam made to coincide as closely as possible with the axis of the collimator opening. A lucite block for eliminating stray electrons was placed next to the primary collimator and attached to it by means of an extension of the front brass

plate. Plastic bolts through this block fasten the collimator to the lower coil box in a fixed position. The height of the collimator is such that small vertical adjustments are possible. Small lateral and rotational changes are achieved by shimming. The alignment is checked by films exposed perpendicular to the beam. This procedure is fairly long and tedious and should not be repeated whenever a new field size is desired. To this end, a collimator was constructed with a cylindrical hole into which inserts determining various apertures fit. The field size can then be varied without moving the main body of the collimator from its position. The laminations of each insert, which are like those in the other part of the collimator, are enclosed in a 6 inch lucite cylinder with 1/16 inch walls. The hole in each insert is tapered in such a way that, at a distance of $7\frac{3}{4}$ inches between the inner collimator surface and the target, the outermost transmitted ray will be parallel to the boundary of the opening. In actual use, this distance was changed to 8 1/16 inches, the inner edge of the hole thus becoming the defining aperture. This was done in order to reduce the formation of secondary electrons by the roentgen rays at the lead surface. This construction was not completely satisfactory when the collimator was used without additional shielding, because the lucite cylinder transmits a distinct shell of rays. In the next collimator built, only a general frame will be fixed in position, and each insert will consist of the complete laminated portion.

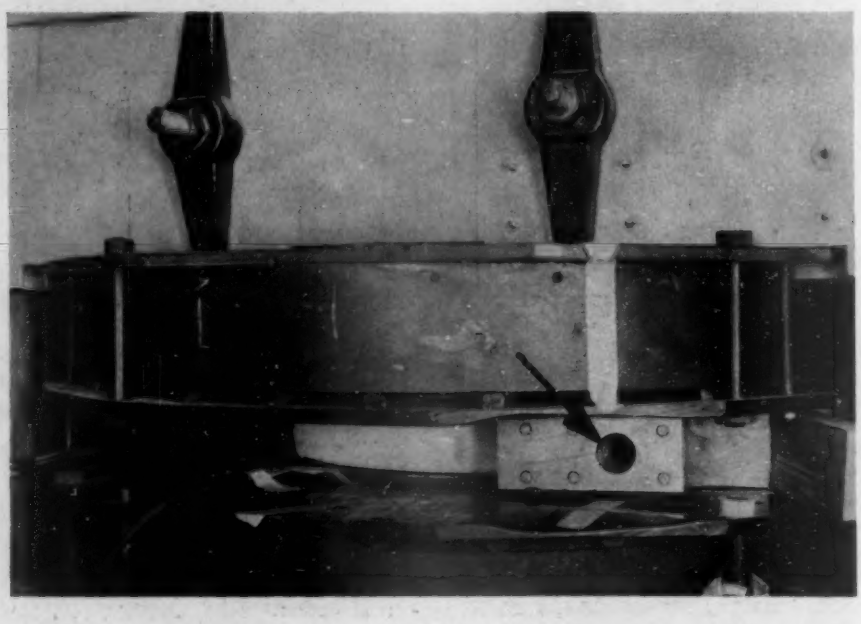


Fig. 9. Collimator old model (arrow pointing to opening) between coil boxes. Porcelain tube behind collimator. Some electron blocks on the right.

We have been using the collimator in combination with a compensating filter (see section 5) which reduces the intensity in the beam to about one-third. This automatically detracts from the effectiveness of the collimator because it triples the ratio of the intensity transmitted by the lead to the intensity in the beam. We found that 6 per cent of the central beam intensity is transmitted through the lead of the collimator. This figure was further reduced by a secondary shield, consisting of a layer of lead bricks 2 inches thick placed just in front of the coil boxes. One of these bricks had a cylindrical hole, lined up with the colli-

mated beam and wide enough so that the beam could just pass through without striking the walls of the opening, which would produce secondary electrons. The secondary diaphragm is shown in the diagram (Fig. 1) and in Figure 10. Obviously, in a permanent installation, apertures of various sizes and shapes must be interchangeable.

The total effect of primary collimator and secondary shield is to produce a very well delimited beam, with a small penumbra of about 6 per cent beam intensity and less than 1 per cent of beam intensity outside the penumbra (Fig. 2). One great advantage of high energy roentgen rays is that the beam stays sharply collimated during its passage through tissue, since lateral scatter is small. This in contrast to low energy rays, where lateral scatter is strong enough to diffuse a beam considerably even though it be perfectly collimated when entering the body. The sharp definition of the beam involves, of course, one postulate: the beam must be aimed with the greatest care, because one cannot rely on the diffusion of the beam to correct slight errors in direction.

5. FILTER: SHAPING OF ISODOSE SURFACES BY DIFFERENTIAL ABSORPTION

At conventional energies, roentgen rays are emitted from the target in all directions with about equal intensity. At high energies, the emission is preferentially in the forward direction of the electrons impinging on the target. For the roentgen rays produced by the 22 mev. betatron, the angle between the central shaft of the beam and the direction at which the intensity is one-half of maximum is about 4° (Fig. 2). This distribution has disadvantages in therapy since it gives a non-uniform dose over the field of application; for example, at a target-skin distance of 75 cm., a 10 cm. field will have a dose at the edge of only

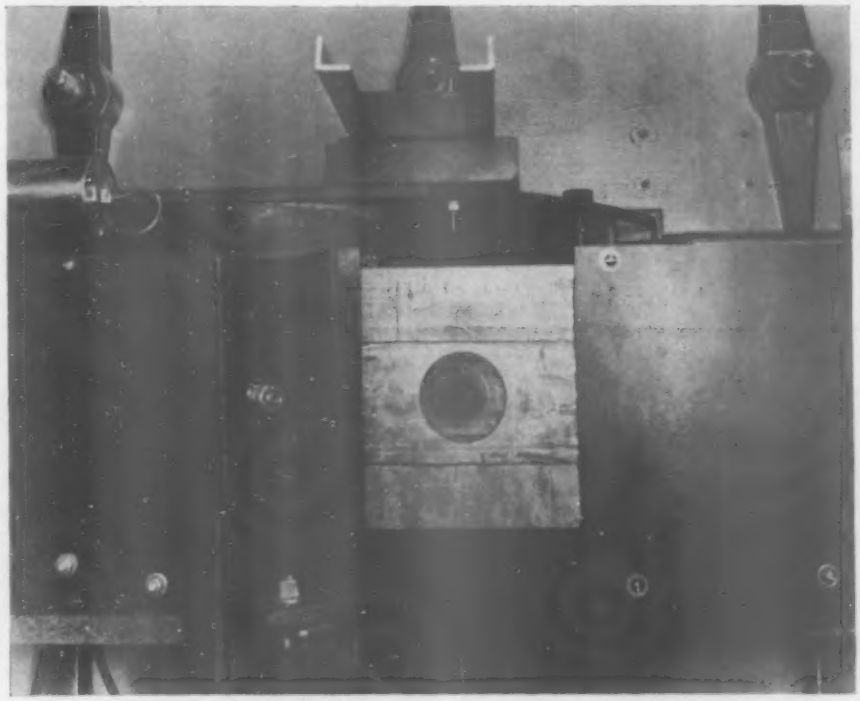


Fig. 10. Compensating filter. The end of the graphite stick protrudes from the collimator opening seen through the hole in the secondary shield.

one-half that at the center. The effect of this concentration of the radiation in the forward direction on the distribution of ionization within a presdwood phantom is shown by the isodose chart of Figure 4.

The variation of intensity over the area of the field is inherently characteristic of the betatron. It could be dealt with by appropriate schemes of crossfiring. However, a more direct and satisfactory solution is suggested by wedge filters and related devices used at conventional energies. We designed a differential absorber to be placed between target and patient in which the thickness for each angle is adjusted to such a value that the emerging beam will be reduced to almost uniform intensity over the entire field. Two obvious additional conditions were that the absorber should improve rather than deteriorate the quality of the beam, and that electrons produced in the absorber should not be allowed to strike the patient.

It is common practice to construct filters, both plain and differential, of heavy metals. This practice is advantageous at energies up to 1 mev. because both photoelectric absorption and Compton scattering are decreasing functions of energy and any absorber will, in general, tend to remove the softer components. However, pair production appears above 1 mev. and is an increasing function of energy. Pair production becomes the predominant process in heavy elements at energies of a few million volts. Thus, absorption in these materials increases with energy, and they are not good filters. Effective filtering of high energy radiation requires the use of one of the light elements, in which the cross section for pair production is low. These facts are illustrated by Table 1, which shows the transmission of various materials for quanta of a definite energy.

The thickness of the filter is adjusted in each case to give 50 per cent transmission for 20.4 mev. quanta. The values for the total absorption coefficients used to calculate the transmission were obtained from W. Heitler.[3] Inspection of the table shows that lead is not a good filter material since it is less transparent to the 20.4 mev. quanta than to quanta of a lower energy (the best penetration in lead is near 4 mev.). Copper absorbs nearly uniformly over the high energy part of the spectrum. Among the materials represented in the table, carbon shows the best characteristics with regard to improving the quality of the beam. Our compensating filter was made of carbon. The filter also produces secondary electrons which are removed by the action of the magnetic field as in the case of the collimator (section 4).

We built one compensating filter for use with a collimator of $7\frac{1}{2}°$ angular aperture. It is made of a piece of graphite, density 1.6, 24 cm. long, and shaped like a cigar to

TABLE I

RELATIVE TRANSMISSION OF VARIOUS MATERIALS

Quantum Energy (mev.)	0.87 cm. Pb	2.3 cm. Cu	12.6 cm. Al	41 cm. H_2O	32 cm. C(d=1.6)
0.25	0.02	0.08	0.026	0.0006	0.004
0.51	0.23	0.91	0.06	0.020	0.012
1.0	0.50	0.31	0.13	0.06	0.04
2.5	0.66	0.45	0.28	0.17	0.14
5.1	0.66	0.52	0.39	0.29	0.26
10.2	0.59	0.53	0.46	0.41	0.38
20.4	0.50	0.50	0.50	0.50	0.50

provide thicknesses varying appropriately with angles. The filter is placed in the opening of the collimator. Construction details are shown in Figure 11, and the alignment, in the schematic drawing of Figure 1, and the photograph, Figure 10. The filter first constructed (and used in treatment) produced a somewhat asymmetric field (Fig. 7). A second filter was built subsequently which gave a field uniform to ± 5 per cent (Fig. 4). Obviously, greater uniformity could have been reached by further adjustments: we did not feel compelled to make these. Greater precision will be worth while when one can count on reproducing exactly the alignment of tube, collimator, and filter.

The effect of the filter on the penetration of the beam is small. Figure 3 shows depth dose curves taken along the center line. It can be seen that, without the filter, the depth dose at 20 cm. is 50 per cent of the peak dose (at about 4 cm.); with the filter it is 55 per cent, an increase of 10 per cent. The increase is smaller at 10 cm.

Another effect which the filter produces is an accentuation of the transition effect from surface dose to peak dose. An indication of this effect can be seen in our curve which begins at a depth of 2 cm. This effect is not pronounced either.

The effect of the compensating filter on depth dose distribution in the direction perpendicular to the central ray is striking, and more than makes up for the loss in dosage rate (the rate was about 30 r/min. with and about 90 r/min. without filter). Figures 4 and 7 show dosage distributions which approximate the proposed goal, viz., isodose surfaces parallel to the surface. One could, of course, build differential absorbers yielding inclined isodose surfaces, or isodose surfaces of a variety of other shapes which might be desirable in the treatment of tumors in specific locations.

6. Elimination of Background Radiation by Shielding

The effective use of the high energy roentgen-ray beam from the betatron requires that the main beam be well collimated and that it be free of secondary electrons. These two conditions have been discussed in the collimator section. A third requirement is that the background stray radiation external to the beam be of low and inconsequential intensity. The stray radiation consists of electrons from the betatron, unabsorbed primary roentgen rays, and secondaries produced in the absorption and scattering of the primary rays by any material placed in the beam. These secondaries are penetrating because they have high energy. They must be reduced in intensity to protect the patient, operators, and instruments.

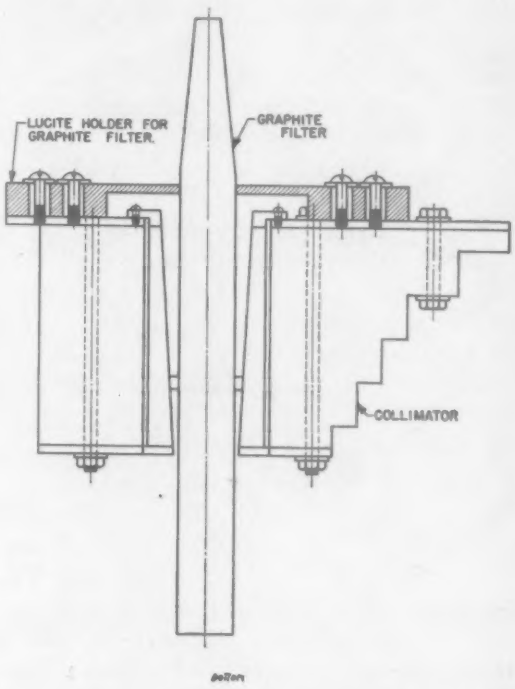


Fig. 11. Compensating filter. Construction drawing. A ring and a lucite holder attach the filter to the collimator. The screws allow slight adjustments of the filter.

Shielding was accomplished by means of masonite die-stock and lead in and around the collimator, and by means of the secondary lead shield. The relative positions are shown in Figure 1. Since the energies of the secondaries are higher than in conventional

roentgen-ray machines, the thickness and the types of material are more critical and a choice has to be made more carefully. For example, because of its atomic number, lead is not the all purpose absorber that it is at low energies. Stray high energy electrons are known to exist in the space surrounding the acceleration chamber. These electrons may be effectively absorbed by

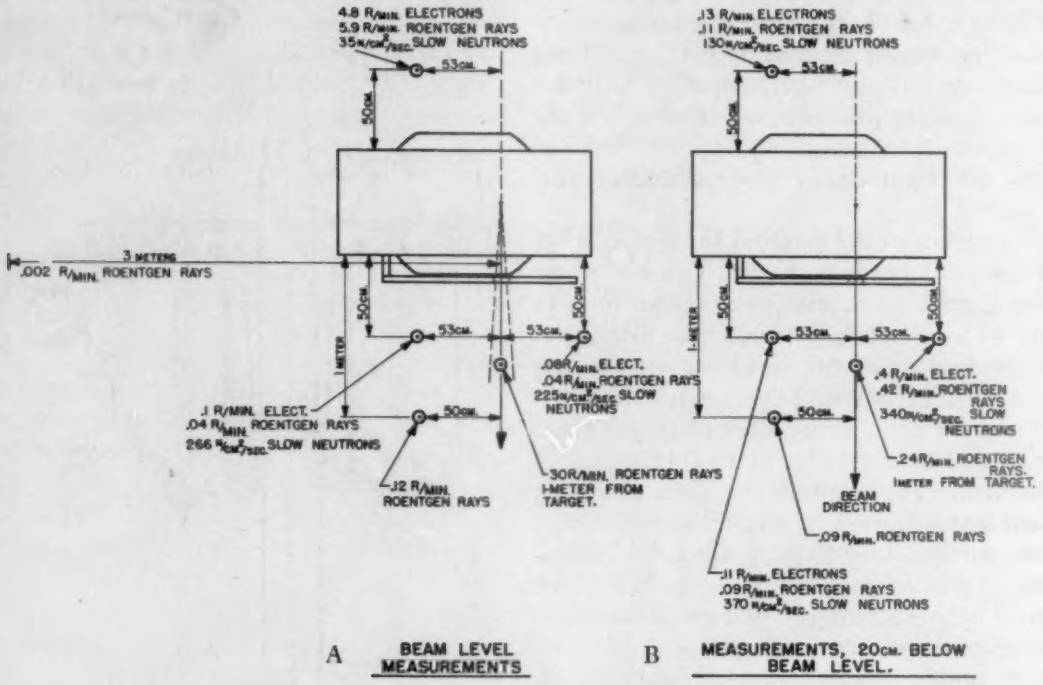


Fig. 12. Stray radiation survey.

placing masonite or lucite blocks in this space. About 5 cm. of masonite are required to stop a 20 mev. electron but, because of the low average atomic number of masonite, few secondary roentgen rays will be formed.

Masonite is also useful because it makes possible the shielding of a third type of radiation which is foreign to all low energy roentgen-ray machines. These rays are neutrons which are produced as a consequence of the high energy of the roentgen rays. Neutrons can be ejected from an atomic nucleus when a quantum of sufficient energy has been absorbed by that nucleus. Since neutrons are not charged, they are absorbed with difficulty when moving rapidly. Some of the neutrons produced at the roentgen-ray target are slowed down by inelastic collisions in the iron of the betatron magnet. Hydrogenous materials were placed in front of the betatron to absorb such slow neutrons. Thus, masonite helps to shield against not only high energy electrons, but also neutrons. In the future, masonite could be used much more liberally than in the arrangement shown in Figure 1.

For the removal of stray roentgen rays the secondary lead shield of Figure 1 was employed. Lead was chosen because of the high absorption coefficient for roentgen rays. The shield was found particularly necessary to eliminate horizontal sheets of roentgen rays. These rays appeared through the space between the lead collimator and the copper of the betatron magnet coils, both above and below the collimator.

A survey of the electron, roentgen-ray, and neutron background doses was made with the betatron arrangement of Figure 1. The electron doses were measured ap-

proximately by means of a 0.25 r Victoreen thimble placed in air. The roentgen-ray doses were measured with the same thimble surrounded by 1.5 inches of wood. The slow neutron doses were measured by detecting the 40 second activity induced in rhodium foils with and without cadmium shielding.

The results of these measurements are shown in Figure 12, *A* and *B*. The measurements shown in Figure 12*A* were made at the beam level and their magnitude for different locations should always be higher than the corresponding measurements taken at 20 cm. below the beam as shown in Figure 12*B*. However, at one location it is seen that the electron and roentgen-ray doses are higher for the 20 cm. below the beam level than those at beam level. This happened because the secondary lead shield of Figure 1 did not extend sufficiently above and below the beam. This can and should be remedied, but was not thought to be serious in the present experimental survey.

The electron and roentgen-ray doses as shown in Figure 12 can be made less than 0.24 r per minute at a distance of 20 cm. off the axis of the roentgen-ray beam whose intensity was approximately 30 r per minute. However, some precaution must still be taken near the patient when the minimum shielding is used. It should be noted that the roentgen-ray dose at only 3 meters from the patient was at the very tolerable level of 0.002 r/min.

The slow neutron doses shown in Figure 12 are lower than the actual slow neutron doses because of the selective energy sensitivity of the rhodium foils. It is believed that the true values are higher than those listed by about a factor of 5. Multiplying the values listed by 5 brings them slightly above 1,500 slow neutrons/cm.^{2}/sec. which has sometimes been considered a tolerance dose for an eight hour day. Recent experiences indicate the safe level may be lower, but the levels around the betatron appear to be safe for the duration of a normal treatment schedule.

No measurement of the fast neutron flux was made at this time. In a previous cloud chamber experiment, the fast neutron flux 3 meters from the target was estimated at 200 per cm.^{2} per second. In a threshold detector experiment a value of about 1,000 fast neutrons/cm.^{2}/sec. was found, also at 3 meters. Such a level would not be safe for an eight hour day, but should be safe for a treatment. A detailed study of the fast neutrons should be made for any given future arrangement. No special difficulty is anticipated in adequately shielding against fast neutrons.

The simple shields described provided sufficient protection. The survey data show that it is easily possible to make the betatron safe for clinical purposes.

7. TREATMENT PLAN

With high energy rays, it is possible to treat any region anywhere in the body with high doses without reaching dangerously high levels outside the predetermined region. It is feasible, and it may be desirable in selected cases, to achieve a caustic or almost caustic effect in the depth. With low energy equipment, this can be done only in accessible regions of the body. For our patient, treatment with high doses to a restricted area was clearly the only possibility. He had previously been given a course of roentgen treatments with large fields and medium dose, with negative results. These treatments had produced radiation sickness, without any evidence of tumor response. Glioblastomas are often not radiosensitive, and the particular one with which we were dealing had already proved that it was not. Hence, the only remaining chance to control it was the administration of very high doses. Since such doses are likely to produce irreparable damage in normal tissue, the region to be irradiated was planned in such a way that, while presumably containing all the tumor cells, it would not extend into portions of the brain where damage to normal tissue would lead to consequences incompatible with a fairly normal life. In other words, we restricted our attention to that part of the

potential tumor-bearing region which we felt we could destroy without incapacitating the patient.

The guides for outlining the tumor area thus defined were the report of the neurosurgeon, the neurologic symptoms, and normal anatomy. This information was not too reliable, considering that the decompression, tumor growth, and reactive swelling were likely to disturb normal anatomical relations in one way or another. On autopsy, our guess was shown to be fairly good; a sphere of 9.5 cm. diameter, located as indicated in Figure 13, did enclose the entire tumor. However, with better knowledge of the tumor location, we could have used considerably smaller fields. In future cases, it might be worth while to make exact measurements on the tumor at the time of operation, and possibly also to insert metal markers to indicate any future displacements.

Fig. 13. Model head. Outlines of brain drawn in. Shaded circle: presumed tumor region. Dark area: tumor as found at autopsy.

In geometrical terms, the problem was to irradiate a sphere (the tumor) situated eccentrically in an approximate ellipsoid (the head). In order to obtain an optimum ratio of dose inside to dose outside the tumor region, as much of the surface area of the head as possible should be used through which to direct beams toward the tumor. The amount of surface available was determined by three restrictions: (1) all caudal approaches were excluded, some because they would contribute too much to the integral dose, some because they were not feasible with a patient who could not cooperate much; (2) the longitudinal angle was restricted by the condition that no beam should reach either eye directly (Fig. 14*A*); and (3) the transverse angle, by the condition that the normal hemisphere should receive as little radiation as possible (Fig. 14*B*). The first two restrictions are obvious; the third was dictated by the fact that the patient had not tolerated previous irradiations involving a large portion of the brain. It might, however, be useful to accept this restriction in general, in order to leave the patient with one almost completely unirradiated hemisphere, especially as this does not exclude depth dose distributions which are very satisfactory, as shown below. The limited amount of time available prevented us from searching for the treatment plan leading to the optimum dosage distribution; instead, we devised a method which, while not the best, still gave a very good distribution of dose, and which could be tested and executed with comparatively simple means. It was decided to use a conical beam of such size that its cross section at the tumor level was slightly larger than the assumed diameter of the tumor. Instead of sweeping continuously with this beam over the allowable area of the head surface, we decided, for reasons of expediency, to use a number of discrete, but overlapping fields. Brief consideration will show that such a method cannot be far from an optimum solution.

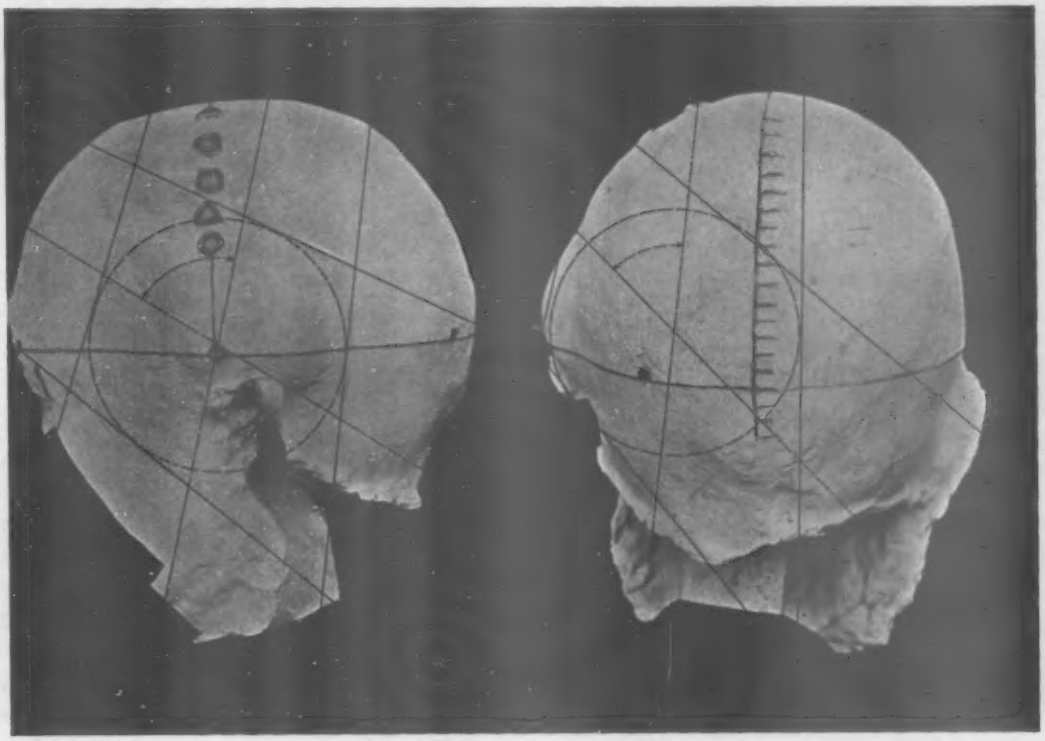
First, the tumor region is irradiated fully by each single field. This guarantees the absence of "cold spots" within the tumor, and minimizes the influence of errors due to faulty aiming of the beam during one or

another treatment. With the limited amount of surface available for irradiation, one obtains a certain dosage gradient throughout the tumor region, the point farthest from the center of the total surface area used receiving the smallest dose. This gradient is reduced even by a moderate sweep in two directions, for each point in the tumor region averages over various dosage levels in the beam, and the differences between these averages are obviously smaller than the differences between points in the depth dose distribution of a single beam.

Second, we shall consider the dosage distribution outside the tumor region. Figure 15 shows some cross sections through regions upon which two, four, and nine beams are incident, in order to illustrate how increasing the number of beam directions used improves the depth dose distribution. For simplicity, cylindrical beams were assumed, and the dose is assumed to be uniform throughout the beam. The tumor is a sphere.

Figure 15*A* shows two beams intersecting at 80°. One sees that the space where they overlap forms a double triangle if viewed in the direction perpendicular to the plane of the angle. It is an ellipse if viewed in the plane of the angle (Fig. 15*B*). The region intercepted by the two beams is a sphere (the tumor) with four pointed caps.

We now add to each beam another beam, rotated 60° in a direction perpendicular to the plane of the original angle. This gives four beams aiming at the tumor from different directions. The region where all four beams overlap is the volume occupied in common by the two intercepts of two



A *B*

FIG. 14. Restrictions on angular sweep. The tumor region is drawn in in photographs of the model head. *A*, longitudinal sweep restricted by postulate that no beam must hit the eye. *B*, transverse sweep restricted by condition that the right hemisphere should receive little radiation.

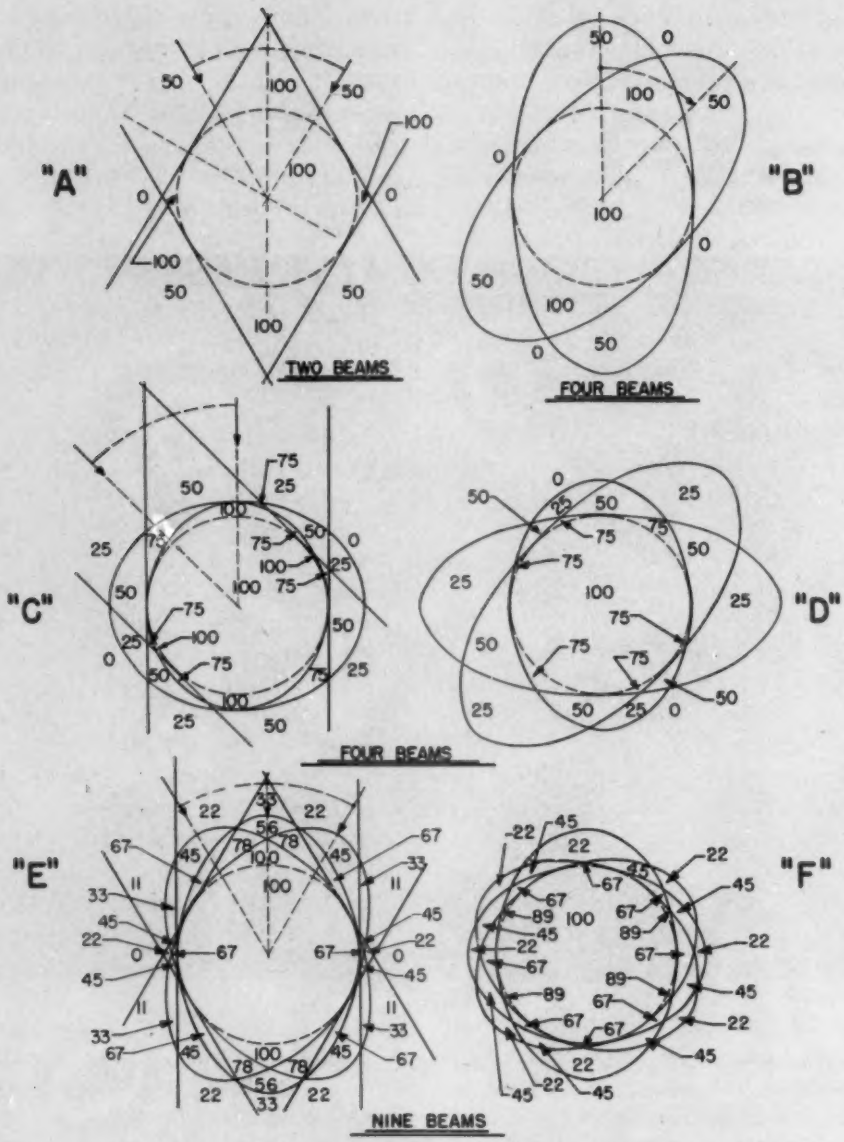


FIG. 15. Multiple beams intercepting a spherical tumor. Assumed allowable sweeps: 80° in one, 60° in the other direction. Numbers: percentage depth dose. The graphs show the formation of "caps" by beam intersection. Three cross sections (through the three-dimensional dosage distribution) are shown for four beams, two for nine beams. Note rapid improvement of depth-dose distribution with increasing number of beams, even though the field of approach is severely restricted. Simplifying assumptions: cylindrical beams, depth dose constant throughout the beam.

beams (Fig. 15*B*). This volume is, again, a sphere with four pointed caps; but each cap being the intersection of two caps, is of considerably reduced size. Figures 15*C* and 15*D* show the same situation viewed in different directions. The percentages given are depth doses, if one assumes that the dosage stays constant throughout the beam. This is not a bad approximation in the case of high energy roentgen rays.

In Figures 15*E* and *F*, additional beams have been interposed midway between the

two angles. This gives a total of nine beams, distributed over the same entrance area. It is seen that the 100 per cent caps have shrunk considerably toward the sphere, i.e. a smaller region outside the tumor is included by all the beams. When the number of fields is increased, caps of lower order become progressively larger, but have progressively smaller relative doses. Thus, the greater the number of fields used, the more the dose delivered is concentrated on the tumor region.

The distribution given in the figures is obviously not the optimum one. It could be improved by staggering the fields in neighboring planes, and also by giving larger doses to the corner fields than to the central ones. A theory of optimum distribution is under investigation at the present time.

In the present case twenty-five fields were used and distributed as follows to give a reasonably uniform dose: A polar axis was defined as a sagittal line passing through the center of the tumor, the poles being the points where this line intersected the surface of the head. An equatorial plane was laid through the center of the tumor region, perpendicular to the polar axis. Meridians were defined as lines, situated in planes containing the polar axis, connecting the two poles. Arbitrarily, the allowable transverse angle was divided into four equal parts, thus defining five meridianal planes. Five fields were placed along each meridian in such a way that the beam axes differed by equal angles at the center of the tumor. The fields along neighboring meridians were staggered.

The overlapping of entrance portals might cause hot spots with low energy rays; at high energies, the surface dose is small because of the transition effect, and one does not have to worry about hot spots near the surface. Doses at the exit portals also are smaller than doses at the tumor level.

8. TREATMENT TECHNIQUE

The method of treatment used required accurate positioning of the head. It was decided to rely on the plaster cast method for keeping a patient precisely in a given position. The taking of a plaster mold was supplemented by making a model of the head. This model was used in experimenting with treatment techniques, and, later on, for alignment of the mold with the beam before each treatment.

The cast and molds were prepared by the Department of Dentistry at the Carle Clinic, by seating the patient upright and molding rapid-setting impression plaster completely around the head. It was necessary to do this in four sections, two lateral, one occipital, and one frontal. Each was allowed to harden slightly, and a separating medium was applied upon the plaster to be "lapped" by the next section.

After the impression had hardened, it was removed and re-assembled, and its interior painted with separating medium. Plaster was used to form the model of the head, and a short length of wood was anchored in the model to act as a support. When the model had hardened, the impression plaster was removed, the model painted with separating medium, and a right and a left mold of plaster were formed, to be used as inserts for the patient's head during treatment. From the plaster model, we made two presdwood replicas for dosimeter tests.

On the plaster head, the two poles of the axis through the assumed center of the tumor and the equator were marked. The intersection with the equator of the five meridians chosen were labelled with shapes of lead wire (Fig. 14*A*). The center of the tumor was marked by a small steel ball cemented at the base of a drilled hole. Lead wire markers were placed in the eyes.

The method of treatment required easy maneuverability of the head along each chosen meridian. To accomplish this, an adjustable head rest was made and mounted on the table described below. The center of rotation of the head rest could be adjusted to coincide with the center of the tumor, and with the center of the beam. The distance from the target was deter-

mined by the desired cross section of the beam at the tumor level and by the size of the collimator opening. In our case, the target distance thus fixed was 87.5 cm. A plumb line dropped from the ceiling marked the point at which the tumor center was to be located. Figure 16 shows the plumb to be in position.

head rest had been mounted was clamped to this platform (Fig. 17). For more general use, it will be necessary to use a platform which is mounted in such a way that the position of the center of rotation can be varied.

A method had to be devised whereby the head rest, with the plaster head in place,

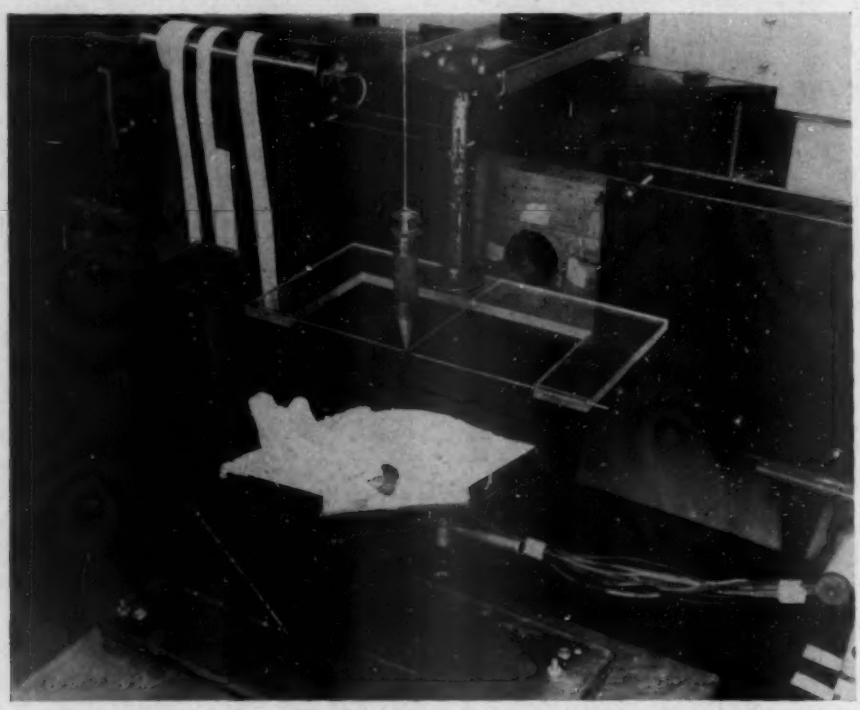


Fig. 16. Aiming device. Three pointers and a plumb-bob are aligned with the center of rotation and the central ray. The plaster mold (below) is moved on the positioning device until the center of the tumor coincides with the point defined by the aiming device.

To position the patient's head, the two molds (one to fit the right and the other to fit the left side of the head) were mounted in brass trays which could be clamped to the adjustable head rest, as shown in Figure 16.

The next requirement was that the patient's body should be able to be rotated easily about the center of the tumor. For this purpose, a steel platform was built and made to pivot about a point directly below the plumb line. Rollers were placed beneath the platform, so that it could be rotated with little effort. The table upon which the

could be aligned so that the central ray impinged upon the selected meridian and passed through the center of the tumor region. A lucite frame was made, shown in Figure 16, with sliding pointers focusing upon the point of the plumb bob, i.e. upon the center of the tumor. To obtain a desired head position it was simply a matter of adjusting the positioning apparatus until two of the pointers were aligned with the polar axis and the third pointer aimed on the equator at the chosen meridian. Figures 18*A* and *B* show this process. The adjustable head rest which is pictured had

to be made in one day, and in spite of its simplicity, fulfilled the requirement. A more desirable positioner would be one in which each direction of motion could be minutely controlled, and independently of the other adjustments.

Figure 17 shows the circular arc which was laid out on the floor and marked to determine the amount of angular sweep along each meridian. This figure also shows pillows which were used to form a bed (inclined to prevent the beam beyond the exit field from passing through the body) and straps which helped to hold the patient in place.

FIG. 17. Arrangement of patient for irradiation. Patient's head immobilized in plaster mold. An inclined bed is formed in order to prevent the beam from traveling through thorax and abdomen. The position of the platform is read by pointer and scale (on the floor). The table is clamped to a rotating platform.

This system of positioning the patient's head proved to be satisfactory in obtaining the accurate alignment needed. The same head rest was used for holding alternately the patient's head or one of the replica heads. Thus, the measurements made on the models corresponded with the actual treatment the patient received.

Thus equipped with positioning devices and a general treatment plan, we proceeded to determine in detail the positions of the five fields along each of the five meridians. The plaster head, equipped with markers, was placed in the head molds in the treatment position, and the line-up of each meridian was checked by roentgenograms which showed the steel ball to be almost exactly in the center of the lead wire figure marking that meridian. The allowable angular sweep (latitude) on each meridian was determined by finding the angles at which the eye markers became visible in a roentgenogram, and then reducing the sweep to a safe amount. To assist in this effort, a series of circular apertures was constructed which could be mounted at fixed distances from each other and from the tar-

Fig. 18. Aligning procedure. The plaster head is placed in the mold, which is mounted on the positioning device. The two lateral pointers are lined up with the end points of the polar axis (dots), and the axial pointer with the intersection of the selected meridian and the equator.

get. The diameters of the apertures were such as to indicate the extent of the collimated beam at that position. This device proved helpful, but the roentgenograms were the reliable test. In the long run, it will certainly be simplest to check both entrance and exit fields with appropriate optical devices.

modate Victoreen thimbles were drilled into critical regions. Wooden dowels filled in those holes not being tested. This model served as the object for calibrating the actual dose to be given (Fig. 19). The other head was equipped with two dowels for holding the many laminations in place. Films were placed between laminations at

FIG. 19. Model head of presdwood for Victoreen measurements. Five holes are drilled into critical regions. Wooden dowels fill the holes not in use. The plaster molds are used for alignment.

To evaluate the proposed treatment plan we decided to rely on integral tests rather than on computations. For the experimental tests, the two replica heads were used; these were made of $\frac{1}{4}$ inch laminations of presdwood with contours shaped at each level by reference to the plaster head. A test with a skull showed that the influence of the bony structures upon depth dose distribution was negligible. Hence, it could be assumed that the depth dose distribution in the presdwood models would closely approximate that in the patient's head. One of the models had the laminations cemented together, and holes large enough to accom-

selected depths and trimmed to the shape of the larger adjacent lamination. The assembled replica was rendered light-tight by two layers of masking tape. The dowels served as fiducial marks in aligning the films in the head. The head was then placed in the mold in the irradiation position and given the whole proposed treatment, the doses being scaled down by a large factor to give measurable film densities.

The densities at 1 cm. intervals over the entire extent of each film were measured. Reduction of the data obtained to percentage dose was accomplished as described earlier. The boundaries of typical levels are

Fig. 20. Tumor region and isodose surfaces. Longitudinal sections through the center of the tumor are projected upon photographs of the plaster model.

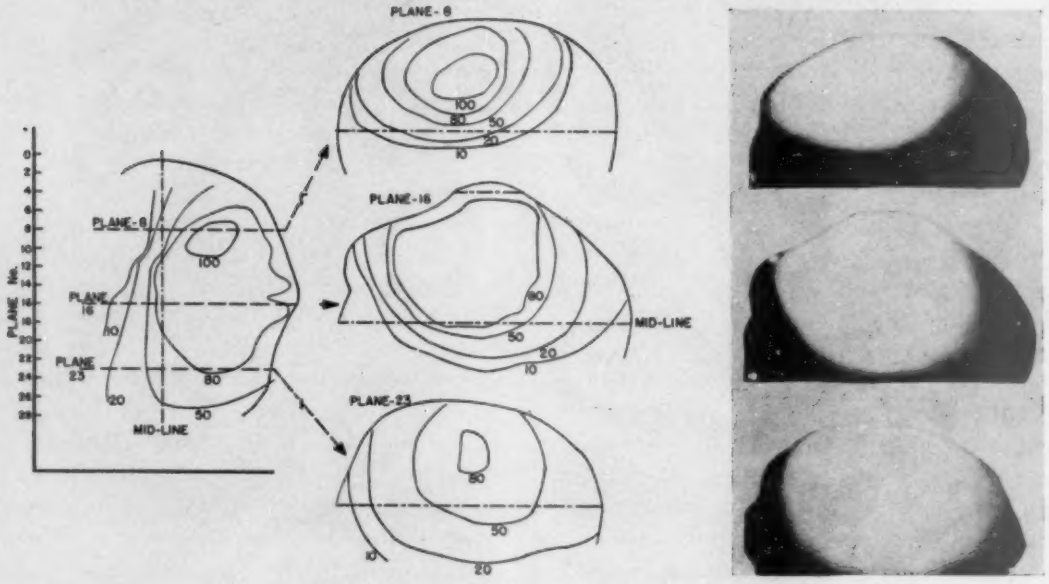


Fig. 21. Dosage distribution in presdwood model head. Left: frontal section through center of tumor showing several isodose levels. Middle row: horizontal sections (number of plane = distance from top of the head in quarter inches). Right row: typical films used for dosimetry.

illustrated in Figures 20 and 21. Lateral sections through the center of the tumor region are given with percentage dose indicated in Figure 20, and horizontal and vertical ones in Figure 21.

Because of the regular pattern of the densitometer readings, the fine detail is not recorded and hence does not appear in the isodose levels drawn, which are the result of interpolation among the actual readings. The fine structural details, i.e. the "caps" described in section 7, are clear in the original film, although the reproduction (Fig. 21) does not show them well.

It cannot be too strongly emphasized that extremely steep dosage gradients are produced by the technique described above. Dosage gradients of about 50 per cent in 1 cm. are common at the boundary of the tumor region. This means that regions containing heavily damaged tissue can exist very close to tissue with relatively small damage. This apparently opens new possibilities for therapy. On the other hand, a fair amount of precision is required in alignment and in dosimetry.

The current of electrons accelerated by the betatron cannot be measured conveniently. As a result, it is necessary to use some means to monitor the dose delivered in each treatment. The means used for this treatment would not generally be expedient except in a laboratory of physics. The method used in roentgenography would be immediately applicable to therapy but the proper details were not at hand.

In the treatment described in this paper, the monitor consisted of a zinc foil (0.002 inch) mounted in the fringing magnetic field of the betatron. The positron activity (2.3 mev. max.) induced in zinc in the reaction $Zn^{64}(\gamma, n)Zn^{63}$ was used to measure the relative number of quanta in the roentgen-ray beam during irradiation. Since this reaction has a threshold of 11.6 mev. and a steeply rising excitation function, it is important that the maximum energy of the roentgen rays generated by the betatron remain constant. During a constant irradiation the number of radioactive zinc atoms at any time t from the beginning is given by the expression:

$$N = k/\lambda(1 - e^{\lambda t})$$

where N is the number of active atoms, k is a constant proportional to the flux of quanta passing through the foil, and λ is the decay constant. In the actual treatment the daily irradiation period was divided into five intervals for the exposure of different fields of the same meridian. Even though these intervals were not necessarily equal in length, as long as they were short compared to the half-life of thirty-nine minutes, the induced activity was proportional to the number of quanta, to a first approximation. This approximation would be even better if a reaction of longer half-life were used, e.g., $Ta^{181}(\gamma,n)Ta^{180}$(8.2 hr.). In the present instance the counting rate obtained with Ta was small for the shortest irradiation interval and thus subject to appreciable statistical errors.

After the irradiation, the activity of the foil was measured and the decay followed over at least one half-life. Initial counting rates of over 10,000 counts per minute were obtained. Specially designed lucite mounts were used to hold the foils in a reproducible geometry, both during irradiation and during counting. The total measured activity A was used to calculate the individual activities A_i contributed by each irradiation interval from the relation:

$$A = \sum_{i=1}^{n} A_i e^{-\lambda \tau_i}$$

where τ_i was the time elapsed between the end of the i'th irradiation interval and the time of counting, and n was the number of irradiation intervals to which the foil was exposed. These A_i were proportional to the actual number of quanta used during the irradiations and constituted an activity index of the dose.

This activity index was calibrated in terms of the dose by comparison with the standard Victoreen thimble located in a presdwood model of the patient's head.

The thimble was so located as to measure the minimum dose delivered to the tumor region. Calibrations were made for all the different meridians used in the actual treatment.

An even more satisfactory monitor would be one which indicated the dosage rate continuously during irradiation, e.g. a flat ionization chamber, which would satisfy the limitations on electrons in the beam. The current from this chamber could also be integrated to indicate the total dose administered. Such a chamber, with walls of thin nylon foil with a conducting coating, has now been constructed.

9. CASE REPORT

Clinical History. The patient was a twenty-seven year old white male in good general condition; a student. His previous history was irrelevant. In August, 1947, he began to have fainting spells, some of them preceded by a queer odor, "like that of gas." He ascribed this condition to overwork. However, he gradually got worse, nervous and irritable; his memory was failing and he was unable to concentrate. On November 11, he sought medical advice. At that time, the neurological examination was objectively negative. The patient was treated with elixir phenobarbital. In December, he had the first of a series of epileptic attacks, some of them preceded by auditory hallucinations and followed by automatisms (driving a hole in the wall). One characteristic episode which occurred at this time was unfortunately revealed only much later: at an examination, he handed in a paper where a perfect first portion was followed by a second portion which consisted of unintelligible scribble. Thus, he had a complete syndrome of temporal lobe affection: uncinate fits, epileptic attacks with auditory hallucinations, and verbal aphasia. However, none of these symptoms were regularly present at that time. An eye examination showed a right upper quadrant incomplete, incongruous, homonymous hemianopsia.

He was referred to Dr. Harold C. Voris, Mercy Hospital, Chicago. An operation was performed on March 20, 1948, and an abstract of the operative report follows: "Left subtemporal decompression with subtotal removal of tumor, Penfield type operation reflecting a musculocutaneous flap. A burr hole was made in the temporal bone and a large decompression was carried out, being careful, however, not to remove bone superiorly or posteriorly beyond the limits of the insertion of temporal muscle. A cannula introduced into the temporal lobe encountered extreme resistance and what was obviously tumor tissue, and the dura was opened in cruciate fashion over the posterior part of the temporal lobe. The tumor was uncapped by removing an approximately 3 cm. square of cerebral tissue. At a depth of about 2 cm., we began to encounter tumor tissue. This tumor at first appeared to be encapsulated, but as our removal proceeded, we discovered that we were really dealing with an infiltrating neoplasm. Areas of the tumor were quite solid and yellowish in color. Other areas were gray-pink and of the relative consistency of brain tissue. A large amount of neoplasm was removed. Except for some anteriorly and superiorly, all gross tumor tissue was removed. Microscopic examination of the tissue removed: It is rapidly growing, pleomorphic and very cellular. In some areas it appears to be sarcomatous and the possibility of primary sarcoma has been considered. However, our final impression is atypical malignant glioblastoma."

Postoperative radiation therapy was given at the Mercy Hospital Institute of Radiation Therapy, Chicago: 800 kv., 10 ma., heavy compound filter, two opposite fields, size 15 by 15 cm. (covering both frontal, temporal, and parietal lobes), 70 cm. focus-skin distance, 33 r/min., 250 r a day, alternating right and left side, for a total of 10 days, March 29 to April 9, 1948. The resulting tissue dose was about 1,700 r throughout the irradiated region. The patient tolerated these irradiations very poorly. His condition, which had improved after surgery, became gradually worse. He vomited a great deal. After ten treatments, the course of radiation therapy had to be stopped.

On April 24, 1948, he was transferred to the Carle Hospital in Urbana, and he stayed here until his death on May 30, 1948. Some of the events occurring during this period are presented in Figure 22.

During the first week of his stay in Urbana, the condition of the patient deteriorated rapidly. His eye sight grew very poor, and he became increasingly stuporous. A neurological examination done at about that time showed abolition of smell and diminished hearing on the left side, very sluggish reaction of the left pupil to light, reflexes generally diminished more on the right

than on the left, weakness of the left side of the face, and of the right leg. There was marked verbal aphasia. A bulge of about 3 cm. height marked the area of the decompression.

Radiation treatment with the betatron was initiated on April 30, 1948. The five fields of one meridian were irradiated each day, the change from one field to the next being accomplished within a few seconds by rotating the table. The doses given in the graph (Fig. 22) are the minimum tumor doses resulting from all five fields irradiated on that day. The maximum doses were about 20 per cent higher. The dosage rate at the tumor was about 30 r/min.

During the first week of treatment, the patient showed slight but definite improvement. He had no indication of radiation sickness. He did not vomit. His lymphocyte count and his granulocyte count decreased somewhat, but not much. His neurological symptoms improved. After about half of the course of treatments had been given, we decided to shift the hypothetical tumor center by 1.5 cm. toward the occiput. (The resulting slight change in depth dose distribution is taken into account only in Figure 23, which shows brain sections with superimposed isodose levels.) On May 11, the patient quite suddenly showed marked weakness. This break was clearly reflected in the pulse curve (Fig. 22). After a few days of increasing weakness, we felt that we could not continue the radiation treatment any further, and stopped at the dose of 4,669 instead of reaching 6,000 r.e.b.a. as originally intended.

The decompression bulge was very tense in the beginning, gradually softer during roentgen treatment, and alternated its consistency very rapidly afterwards. Also, the width of the pupils fluctuated considerably.

The weakness increased steadily, and the patient grew more and more stuporous. Terminally, he developed pulmonary congestion. He died on May 30, 1948.

Autopsy. The following is abstracted from the autopsy report. On the left temporal aspect of the skull there was a soft bulging mass measuring roughly 6 by 5 by 3 cm. in its major axes, rounded and fluctuant. On the skin over it was an arcuate recent, but well healed surgical incision, and, around the ear, some brownish discoloration such as follows irradiation. The head was hairless.

The right lung weighed 900 gm. There was diminished crepitus throughout, and the lower and middle lobes were heavy and darkly congested with blood. The cut surface dripped water on light compression, was brownish-gray in color and showed slightly accentuated bronchiolar markings. The left lung weighed 825 gm.; it too, was heavily congested, moist, and,

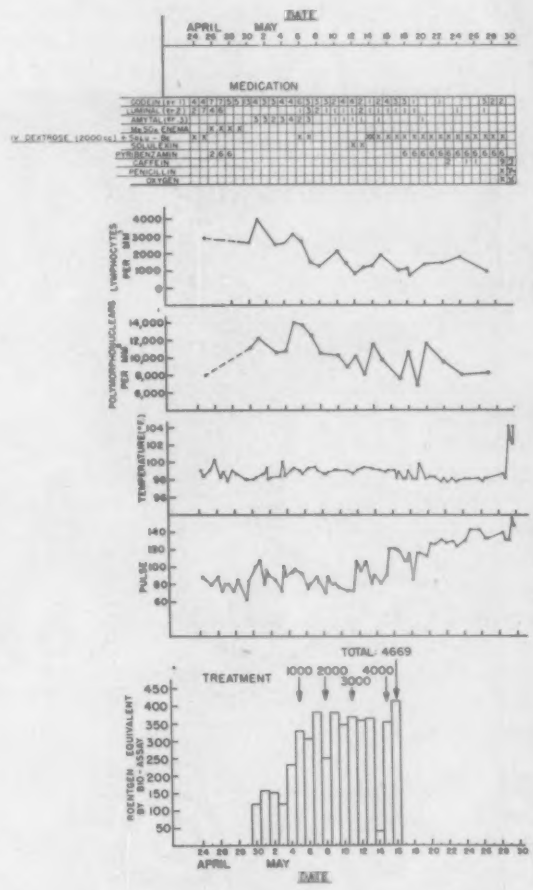


Fig. 22. Clinical record including the period of the second series of radiation therapy (betatron). Note little evidence of systemic radiation effect on white blood cells; onset and development of weakness shown by change of pulse frequency. Reduced need for sedation with increasing weakness. Terminal temperature rise due to pneumonia. Roentgen-ray doses were increased as tolerance was shown. Small dose on May 14; treatment interrupted because of inability of patient to cooperate.

in its lower lobe, almost airless. Both lungs showed light apical scars.

The other internal organs were not unusual.

On reflecting the skull, it was apparent that the tumor mass described was a cyst bulging through the bony defect following temporal craniotomy. The external wall of the cyst was

composed of scalp, fascia, and dura all fused. About the margins of the bone defect, brain substance was everted and adherent. There was an excavation in the temporal lobe of the brain which formed the bulk of the cystic cavity, and it was thought at autopsy that the cyst probably communicated with the posterior horn of the lateral ventricle. The cyst was lined by a tough organized membrane with a smooth, glistening internal surface, and filled with pale yellow, slightly opalescent fluid.

The leptomeninges around the circle of Willis were somewhat thickened and opaque. No gross vascular damage was noted. Elsewhere, the leptomeninges and blood vessels were not remarkable. The left hemisphere bulges and displaces the midline to the right. In the left temporal lobe is a collapsed cyst, which runs from the temporo-parieto-occipital function forward and is roughly 5 by 4 by 3.5 cm. in its major axes. On the mesial aspect of the cyst the membrane is lost, and friable tumor tissue forms the mesial wall. It is thought that the posterior horn of the lateral ventricle probably communicates with the cyst, and a rather restricted opening into the body of the ventricle is noted (there could have been intermittent drainage from the cyst through this constricted opening). About the posterior mesial pole of the cyst, some yellowish tumor tissue is seen which involves the meninges locally and is adherent to the anterior pons and mid-brain in that area. Anteriorly, the cyst ends in a tumor mass. The meninges are locally adherent and possibly involved in the tumor. The tumor is pinkish-gray in color and contains areas of dark brown and bright yellow pigmentation. It is moderately well demarcated from surrounding brain. In the

Fig. 23. Brain sections each about 1 cm. thick. On two sections, some of the isodose levels have been inked in.

left hemisphere over the parietal lobe, the gyri are widened and flat and the sulci are shallow. A cut in this region shows local cerebral edema.

Beginning at the anterior pole, the brain is cut in sections approximately 1 cm. in thickness (Fig. 23). On sectioning the septum, it is seen that there is distortion of the ventricular system with displacement towards the right. There is slight dilatation of all the ventricles. The remaining tumor involves the whole of the temporal lobe anteriorly and compresses the anterior portion of the striate body. Further, posteriorly the thalamus is invaded by the tumorous mesial wall of the cyst.

Microscopic Examination. Brain: The neoplasm shows three outstanding features: (1) great pleomorphism of tumor cells, varying from small rounded or unipolar cells through larger spindle-shaped cells, and to large bizarrely shaped cells with hyperchromatic or multilobular giant nuclei. Mitotic figures are not numerous; (2) abundant vascular proliferations, both of endothelial and adventitial cells, often to the point of obliterating the lumen; (3) extensive tumor necrosis. The tumor invades adjacent tissue by diffuse proliferation accompanied by proliferation and hypertrophy of local glial cells. It also has a marked tendency to grow along and infiltrate the leptomeninges on the brain surface and to grow along blood vessels. There is some tendency for neoplastic cells to palisade about blood vessels. A few blood vessels are thought to have tumor cells invading their lumina.

Considering the characteristics noted above, the tumor is thought to be a glioblastoma multiforme.

A section through a heavily irradiated region of the brain showed no striking changes, seen with the hematoxylin and eosin stains. There is evidence of glial swelling, which may in part be postmortem change. The Virchow-Robin spaces are widened and there is a suggestion of local astrocytic proliferation about them. Cytologic alteration of neurones cannot be accurately gauged, but there does not seem to be any chronic damage.

We did not attempt a complete analysis of irradiation damage to normal brain tissue, though blocks were taken for such examination. Any damage found might have been due to one of three causes: The surgical trauma, the first course of radiation therapy (with a conventional machine), and the second course (with the betatron). We did not feel that it would be possible to separate these components.

Lungs: The pathologic areas, especially in the lower lobes, show several types of change: there is marked hyperemia throughout. Most of the alveoli are dilated and contain pigmented phagocytes, some multinuclear. The alveoli also contain mononuclear inflammatory cells, often of varying large numbers of granulocytes, and sometimes fibrin, and red blood cells. Many of the bronchioli are filled with mucopurulent exudate. In some sections, the lungs are truly consolidated, and the inflammation approaches that of a purulent pneumonitis in severity. Sections through the upper lobe show less severe changes, often only pulmonary edema. A few scattered small blood vessels contain clusters of what may be degenerating tumor cells.

Heart: There is separation of the myocardial fibers by loose, possibly edematous connective tissue. The fibers themselves show slight loss of staining quality and swelling, with suppression of cross striations in some places. Some of this may be postmortem change, but one has the impression that there was antemortem cloudy swelling as well.

Kidneys: Aside from moderate swelling of cells in the convoluted tubules, no changes are noted.

Spleen: The sinusoids are moderately congested with blood. Occasional small arterioles show hyalin change.

Adrenals: There is swelling and vacuolization and actual loss of parenchymal cells in the outer zona fasciculata, and especially in the zona glomerulosa. In the latter, one sees the pseudoalveolar configurations said to occur in adrenal cortical "exhaustion."

Thyroid: Save for variability in the intensity of staining of colloid, no striking changes are seen.

Liver: The hepatic cord cells show slight loss of stainability, otherwise no pathologic change is noted.

Pituitary: Large numbers of basophilic cells are present, but their concentration as compared with eosinophilic cells varies in different areas in the section.

Testis: Spermatogenesis is generally suppressed, though not absent. No other changes are noted.

Anatomic Diagnoses: (1) Bilateral pulmonary edema; pulmonary congestion; confluent

purulent pneumonia and bronchitis. (2) Glioblastoma multiforme of the left temporal lobe with cyst formation and moderate internal hydrocephalus. (3) Adrenal cortical degeneration.

Discussion. On several occasions during the work on this case we were confronted with a very definite lack of knowledge of a type which can and should be corrected by investigations suggested by our experience.

1. Localization: Our estimate of the extent of the tumor was based on somewhat unreliable data. Consequently, the region irradiated was larger than would have been necessary.

If a conference with the neurosurgeon before the surgical intervention had been possible, means could have been devised which would have enabled us to be more certain about the region to be irradiated. Exact measurements taken during surgery would be helpful. Also, it might be worth while to insert markers at strategic points, so that subsequent changes in position could be recorded on roentgenograms.

2. On autopsy, a large cyst was found with tumor growing on a portion of the cyst wall. The presence of this large cyst was a surprise to two experienced neurosurgeons. Had we known that we could have found clear fluid 4 mm. below the surface of the skin, we certainly could have achieved a decompression by simple needle puncture, and this possibly might have changed the outcome. We had considered the possibility of a large cyst, but its existence was thought to be very unlikely, and hence we did not take the risk involved in puncture. It is possible that the presence of the cyst could have been established by means of radioactive phosphorus, as used by Corrigan. In general, it will be important to know whether its occurrence was merely due to some particular disturbance of the ventricular system, or whether the presence of such a cyst could be expected in this given situation of glioblastoma treated very concentratedly with high doses.

3. The dosage delivered to the patient was too small to eradicate the glioblastoma completely. The plan had been to deliver 6,000 r.e.b.a., but the alarming development of weakness in the patient kept us from carrying out this intention. We did not know the extent of danger of acute radiation death after daily irradiation of sizeable areas of the brain. This uncertainty kept us from going to higher doses when the patient developed symptoms of exhaustion, even though his blood count showed no alarming sign of radiation damage. There is ample information about experiments regarding the consequences of a single irradiation, but we have not found reports on experiments with daily irradiations of parts of the brain in a manner corresponding to clinical treatments. A series of such experiments has now been started.

It is conceivable that, with higher doses, and relief of the pressure by puncture, the patient might have been saved.

10. Appraisal of Possibilities of the Betatron

The deep penetration of high energy roentgen-ray beams leads to very efficient depth dose distributions for the treatment of deep-seated cancers. By efficiency is

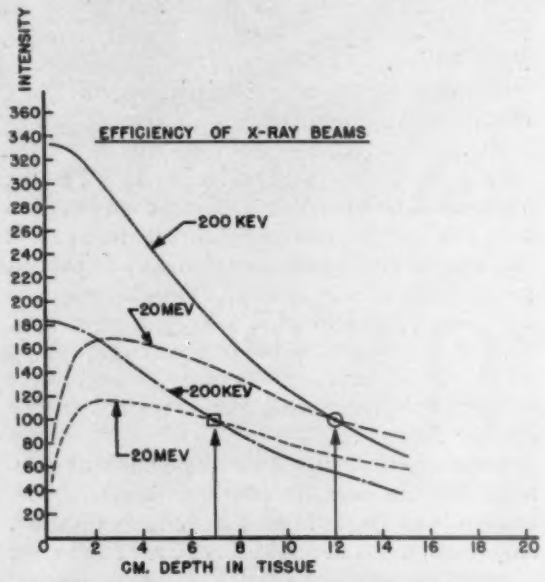


Fig. 24. Efficiencies of high and low energy beams are compared by normalizing exposure at two different depths.

meant here the ratio of tumor dose to highest local dose. Figure 24 illustrates the gain in efficiency with the betatron. One pair of depth dose curves is normalized at a depth of 7 cm., the other at 12 cm. The dose at 7 cm. is 55 per cent of the maximum tissue dose for 200 kv., the maximum dose being at the surface. For 20 mev. roentgen rays, this value is 86 per cent, the maximum dose here being at a depth of about 3 cm. Normalizing at 12 cm. the 200 kv. efficiency is 30 per cent, which is too little to be of much use; at 20 mev., it is 60 per cent, which is still satisfactory.

In general, with high energy roentgen-ray beams the ratio of tumor dose to highest local dose depends little on the depth of the tumor, which is not true for conventional energies. Hence one can use entrance fields which would be uneconomical at conventional energies because the skin-to-tumor distances would be too large. Furthermore, it has been pointed out before (section 4) that the field size of a high energy beam can be made as small as desired without marked changes in dose distribution, and therefore without loss in efficiency. It follows that the number of efficient beams available for cross-firing is much higher with high energy rays. The total gain in efficiency obtained in a system of cross-firing is, then, considerably beyond the gain obtained with a single beam.

In the case presented in this paper, it was shown how a very concentrated irradiation of a given region can be obtained in spite of severe restrictions imposed upon the fields of approach; and the irradiation scheme, as was mentioned, is not the optimum one for the given situation. It can easily be seen that the betatron offers good methods for tumor regions of any shape and in any position in the human body. In general, with high energy roentgen rays it will be possible to irradiate any tumor region without delivering high doses anywhere outside the tumor region.

High energy roentgen rays, whether produced by the betatron or other machines, give us the possibility of nearly perfect geometric selectivity. In order to realize this possibility, one must use precision methods of aligning the patient with the beam. For such methods one can draw on the outstanding work of the British school. A number of adequate methods have been developed and used in practice for years. Most radiologists in this country have been reluctant to adopt methods of precision aiming. However, the use of a well controlled method of aligning the patient with the beam will be compulsory in conjunction with high energy roentgen therapy, and this requires more work than is involved in routine methods used at conventional energies.*

There are, of course, limits even to the best type of external radiation therapy. One of these is our imperfect clinical knowledge of the precise outlines of the cancerous region in any given case. Another is given by excessive aggregate size of the tumor region, especially in cases with metastases. If such large portions of the body are involved that an effective dose cannot be applied without serious danger, the best geometric selectivity will not be of value. Thirdly, in many cases we find normal structures, which must be preserved, in such close association with cancerous tissue that the dose delivered must be dictated by the tolerance limit of these healthy structures; and this limit might be below the destructive dose for a given tumor.

Within these limitations, we feel that the improvement in geometrical selectivity should yield some clinical gains, both in regard to an increased number of cures and in decreased cases of radiation damage. Admittedly, it is not possible at this time to predict just how much can be gained in either respect. The final appraisal can be given only after adequate clinical tests.

A statement concerning the optimum

* We spent about 2,000 man-hours in the treatment of the case reported here. Of course, a large portion of this time was spent on development work which will not have to be repeated. It is expected that the elaboration of techniques for various regions of the body might consume considerable time; repetitions will be much easier. But even when all things are standardized that can be, the amount of work per patient will never be as low as with the routines which are presently in almost general use.

energy range is not out of place here. The radiation used in this paper was the 20 million volt roentgen-ray beam from a betatron of a type which is commercially available. We believe the depth dose characteristics would not be impaired unduly at 15 million volts, but the beam intensity at this energy from the available betatron leaves something to be desired. We have not been able to investigate energies appreciably in excess of 20 million volts. However, certain statements with good physical foundation can be made which lead to the conclusion that too high an energy is possible. These include, as the energy is increased:

(1) The secondaries become more penetrating than the primary beam: the lateral scattering will increase.

(2) The beam becomes more sharply peaked along the central ray: drastic compensating filters would be required.

(3) The transition effect places the ionization peak deeper, possibly deeper than desired.

(4) Annihilation radiation (largely lateral) becomes increasingly more intense.

(5) The number of atomic nuclei artificially activated by the beam increases rapidly. In the case of roentgen-ray activation, the activity is usually positrons with a few million electron volts of energy. These could contribute appreciably to the dose; the activated nuclei could also be transported elsewhere in the body in the blood stream.

The above discussion does not include all the medical possibilities of the betatron. For example, the application of a high energy electron beam which can be obtained from the betatron[11] has not been dealt with at all.

SUMMARY

1. It is likely that the biological effects of high energy roentgen rays are very similar to those of conventional rays, except for differences due to dosage distribution.

2. The dosimetry of high energy roentgen rays is discussed, and a practical unit for clinical use is defined.

3. Several three-dimensional depth dose distributions are given.

4. A collimator to produce a beam of a given cross section is described.

5. A compensating filter to equalize the intensity distribution across the beam is described.

6. Problems of shielding and protection are discussed.

7. A plan for cross-firing a tumor in the temporal lobe is developed.

8. Techniques for executing and testing the treatment plan are given.

9. A case of glioblastoma, treated with the betatron, is reported.

10. A tentative evaluation of the possibilities of high energy rays in cancer therapy is given.

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DISCUSSION

Kenneth E. Corrigan, Ph.D., Detroit, Mich. This paper by Dr. Quastler and his associates is one that is hard to discuss without becoming lyrical, because it is doubtful that any society has ever heard a paper which as a whole represented so much in the way of real advance in knowledge, real scientific acumen and real scientific daring. I doubt that any further detailed discussion by me is indicated.

THE ROLE OF NITROGEN MUSTARD (HN2) AS A SYSTEMIC ADJUNCT TO THE RADIATION THERAPY OF CERTAIN MALIGNANT DISEASES*†‡

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IT IS generally agreed that radiation is the most effective therapeutic agent for Hodgkin's disease, lymphosarcoma and the chronic leukemias. However, at unpredictable intervals in the inexorable progress of these diseases, irradiation becomes unfeasible or ineffective, because of radioresistance, advanced general spread and severe constitutional symptoms. At these intervals, a systemic adjunct to radiotherapy would be most welcome to the therapeutic radiologist, who is generally charged with responsibility for the management of these patients.

In 1946 the early work of Gilman, Goodman, Jacobson and their co-workers[4,5,7] with nitrogen mustard (HN2) in human lymphomas stimulated our interest in determining whether this new therapeutic agent would be a useful adjunct in the radiation treatment of malignant lymphomas, leukemias and certain other malignant disorders.

The Radiation Clinic began this study in January, 1947, in collaboration with the Committee on Growth, National Research Council. We employed HN2, methyl-bis (beta-chloroethyl) amine hydrochloride, a nitrogen derivative of mustard gas, the lethal weapon of World War I. HN2 is a systemic toxin with special selectivity for the blood forming organs, the gastrointestinal tract and proliferating tissues. In therapeutic doses it differs from local roentgen therapy in its severe systemic toxicity, rapidity of action (two to five minutes), narrow safety margin and inability to entirely eradicate local malignant lesions.

There has been a striking dearth of histopathological data to explain the clinical effects of HN2 on human neoplasms. A most important advance in our understanding of these effects has been made by Spitz,[14] who studied at postmortem the tissues of 56 patients treated with nitrogen mustard (HN2) at the Memorial Hospital, New York City. She revealed nuclear and cytoplasmic pathologic changes in lymphomatous lymph nodes somewhat similar to those found after roentgen therapy. In particular, there was observed ballooning of the cells, vacuolation of the cytoplasm and swelling of the nuclei with final fragmentation and ingestion by macrophages. Although there was a general reduction in cellularity, tumor cells survived, growing large and pleomorphic.

CLINICAL MATERIAL

Our clinical material (Table 1) is represented by a group of 87 patients receiving irradiation for a variety of malignant diseases, but principally Hodgkin's disease, lymphosarcoma, chronic leukemia and bronchogenic carcinoma; the latter were included because of reports of clinical benefit by other investigators,[19] collaborating with the National Research Council. These patients had been followed for from three to twenty-one months at the time of this report.

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INDICATIONS

Nitrogen mustard (HN_2) was employed at those intervals in the radiation treatment of the above conditions when, in the opinion of the therapeutic radiologist, irradiation was ineffective or unfeasible, because of true radioresistance, advanced general spread of disease, severe systemic symptoms, acute mediastinal compression, or intractable radiation sickness.

CONTRAINDICATIONS

The contraindications are: (1) severe persistent leukopenia or thrombocytopenia; (2) direct evidence of progressive and severe bone marrow depression; (3) bleeding tendency—to avoid hemorrhage in strategic areas such as the brain, if the patient should vomit during nitrogen mustard treatment.

TABLE I

CLINICAL MATERIAL*

Diseases Treated	No. Cases
Hodgkin's disease	33
Lymphosarcoma	6
Reticulum cell sarcoma	4
Giant follicular lymphoblastoma	1
Mycosis fungoides	2
Acute lymphatic leukemia	1
Chronic lymphatic leukemia	4
Chronic myelogenous leukemia	2
Bronchogenic carcinoma	16
Other malignancies†	18
TOTAL	87

* All cases histopathologically proved.

† These comprised advanced neoplasms of—nasopharynx 3, brain 4, testicle 2, breast 1, rectum 1, kidney 1, bladder 1, nasal fossa 1, liver 1, abdominal metastases 1, malignant melanoma 1, and sympathicoblastoma 1.

DOSAGE

The drug was given intravenously in courses of 0.1 mg. per kilogram of body weight, once daily for four consecutive days. A course was repeated as necessary, but not earlier than at four week intervals, or until the initial leukopenia produced by the drug was no longer present. The maximum number of courses given to any patient did not exceed five (2.0 mg. per kilogram of body weight).

TECHNIQUE OF ADMINISTRATION

Immediately before intended use 10 cc. of sterile, normal saline is injected into a glass vial containing 10 mg. of the crystallin salt, thus creating a solution of 1 mg. of HN_2 per cubic centimeter. The appropriate dose is at once withdrawn and immediately injected in the rubber tubing of a running infusion of normal saline. This technique is far more satisfactory than direct intravenous injection, since with the latter technique a chemical phlebitis may be produced. When contamination of the mucous membrane or skin with the solution occurs one should wash the area at once with water because of the vesicant action of the drug.

TOXIC REACTIONS

Local—*Local necrosis* of tissue may occur whenever there is extravasation of the drug. After repeated injections phlebothrombosis and thrombophlebitis may occur. These may be avoided if the injection of HN_2 is not performed in extremities where the circulation is obstructed by proximal tumor masses or large lymph nodes.

General—*Gastrointestinal symptoms*, particularly nausea and vomiting, were encountered in the majority of the cases after the first dose, beginning from one to eight hours after the first injection. These complaints were less common in subsequent injections but were sometimes severe and distressing. It is of interest that there has been noted no alteration in the epithelial cells of the mucosa of any part of the gastrointestinal tract after nitrogen mustard therapy, although evidence of purpura was a frequent finding.[14] The therapeutic agents usually employed to combat radiation sickness appeared to have no influence on "nitrogen mustard sickness." Our patients were not benefited by the use of desoxycorticosterone acetate (a synthetic adrenal

TABLE II

COMPOSITE RESULTS

First Course		Remissions			
Diagnosis	No. cases	No. cases	Per cent	Days average	Days range
Hodgkin's disease	33	28	85	48	7–180
Lymphosarcoma	6	2			19 and 145
Reticulum cell sarcoma	4	2			7 and 82
Giant follicular lymphadenopathy	1	0			
Mycosis fungoides	2	1			21
Acute lymphatic leukemia	1	0			
Chronic lymphatic leukemia	4	1			5
Chronic myelogenous leukemia	2	1			5
Bronchogenic carcinoma	16	9	56	27	5–72
Miscellaneous neoplasms	18	0			
Second Course					
Hodgkin's disease	13	8	61	47	11–101
Lymphosarcoma	1	1			30
Reticulum cell sarcoma	1	1			28
Mycosis fungoides	1	0			
Third Course					
Hodgkin's disease	5	4		33	
Fourth Course					
Hodgkin's disease	1	1		30	
Fifth Course					
Hodgkin's disease	1	0			

cortical hormone) which we have found to be effective in relieving the nausea and vomiting of radiation sickness in 37 out of 50 patients.[3] Preliminary sedation and administration of nitrogen mustard after an overnight fast appeared to be somewhat helpful in avoiding the gastrointestinal symptoms.

The *hemopoietic changes* offer the most important evidence of the severe systemic toxicity of HN2. For the blood-forming organs this drug is a cumulative potent toxin, inducing progressive hypoplasia of the bone marrow with repeated therapeutic courses. In our series 65 per cent of the patients exhibited a leukopenia after the first course. After an interval of four weeks the total leukocyte count usually returned to normal and a second course of nitrogen mustard therapy was delivered if indicated. As the number of courses increased, the leukopenia action became progressively more severe and was accompanied in some cases by irreversible thrombocytopenia and anemia prohibiting further treatment. Penicillin was employed when the leukocyte count reached low levels, and as yet, no case of overwhelming infection accompany-

ing agranulocytosis has been encountered. The dynamic changes in the peripheral blood are noted in Table III. It is of the utmost importance that blood studies be made regularly and the collaboration of a skilled hematologist is helpful. In our studies blood counts were performed daily during nitrogen mustard therapy and three times weekly thereafter until the pretreatment leukocyte levels were attained. Bone marrow biopsies from sternum or vertebral spines were taken at intervals. The dynamic changes in the bone marrow are noted in Table IV. Surgical biopsies, whenever possible, were made before and after treatment. The studies of bone marrow, surgical material and postmortem findings will be critically evaluated and reported in a subsequent paper.

The investigations of Spitz[14] have assisted materially in our understanding of the effect of nitrogen mustard on the hemopoietic system. She has reported that 15 out of 22 cases, excluding leukemias and those bone marrows involved with lymphoid tumor, showed a moderate to severe

TABLE III

PERIPHERAL BLOOD EFFECTS AFTER HN2

Blood Element	Depression Period	Recovery Period
Lymphocytes	1st–8th day	2nd–4th week
Total leukocytes	1st–21st day	3rd–4th week
Erythrocytes and hemoglobin	2nd week	5th week
Platelets	3rd week	5th week

hypoplasia of the bone marrow in doses of 0.2 to 2.8 mg. per kilogram of body weight. All of these cases exhibited purpuric manifestations clinically and at postmortem. A progressive and apparently cumulative hypoplasia was noted in these patients, proportional to the size of the total dose and to the rapidity with which courses were repeated. After multiple courses almost every case showed rather extreme hypoplasia and almost complete aplasia. In these cases hemorrhages, edema and diffuse myxomatous changes were present. Our own preliminary studies of bone marrow tend to support these findings.

A *toxic psychosis* lasting three weeks after a single course of mustard HN2 was

TABLE IV

BONE MARROW EFFECTS AFTER HN2

Bone Marrow Element	Depression	Recovery
Total nucleated cell count	1–3 weeks	3–4 weeks
Blast forms	1 week	2 weeks
Promyelocytes	1 week	2 weeks
Myelocytes	1–2 weeks	3–4 weeks
Metamyelocytes	1–2 weeks	3–4 weeks
Polymorphonuclears	3 weeks	5th week
Erythroid series	1st week	3–6 weeks

observed in one our patients with Hodgkin's disease. This case will be reported in detail elsewhere. As far as we know, this is the only such incident reported after the use of the methyl bis compound. However, Burchenal[1] has found another congoner, SK 137, to cause this complication. The use of SK 137 was discontinued because occasional transient toxic psychoses of twelve to seventy-two hours' duration were noted.[2]

Testicular atrophy induced by nitrogen mustard was reported by Spitz[14] in a paper published in September, 1948, soon after the completion of our research study. In 27 out of 30 males, sixteen to sixty years of age, there was observed complete absence of spermatocytes and spermatids with atrophy of the tubules from which recovery seldom occurred. Only 3 out of 30, or 10 per cent, showed active spermatogenesis after nitrogen mustard therapy. In a control group of 30 lymphomas and leukemias treated by methods other than with nitrogen mustard 16 (57 per cent) revealed testicular atrophy. It would appear to be of interest to undertake a testicular study of our surviving cases employing aspiration biopsy,

surgical biopsy or ejaculation for evidence of testicular damage. We intend to review critically the postmortem testicular findings in our deceased patients and in controls, to be reported elsewhere.

RESULTS

Hodgkin's Disease. It was in Hodgkin's disease—radioresistant, advanced, generalized, with severe constitutional symptoms—that HN_2 was found to be most useful. It will be noted in Table II that 85 per cent of such cases were materially benefited after a single course of nitrogen mustard therapy and their remission lasted from one to sixteen weeks, averaging seven weeks. Table II can hardly portray the dramatic clinical improvement in some patients, grateful for a respite, however brief and fleeting, from extreme discomfort.

A favorable subjective response was measured by relief from fever, night sweats, loss of appetite, weakness, weight loss, pruritus, cough, dyspnea and bone pain. A favorable objective response was gauged by regression of peripheral and mediastinal lymph nodes ((Fig. 1); disappearance of pericardial and pleural effusions (Fig. 2); regression of pulmonary infiltration and atelectasis (Fig. 3); reduction in hepatosplenomegaly and relief from compression of the superior vena cava (Case 1). As a rule, regression of positive roentgen findings paralleled symptomatic improvement, but not always was this so. Indeed, occasionally, it was most surprising to discover roentgenographic evidence of progression of disease even though the patient appeared to enjoy a period of complete relief from symptoms. As the number of courses of treatment was increased there was a diminishing response to nitrogen mustard therapy, until ultimately, there was evidence of "nitrogen mustard resistance."

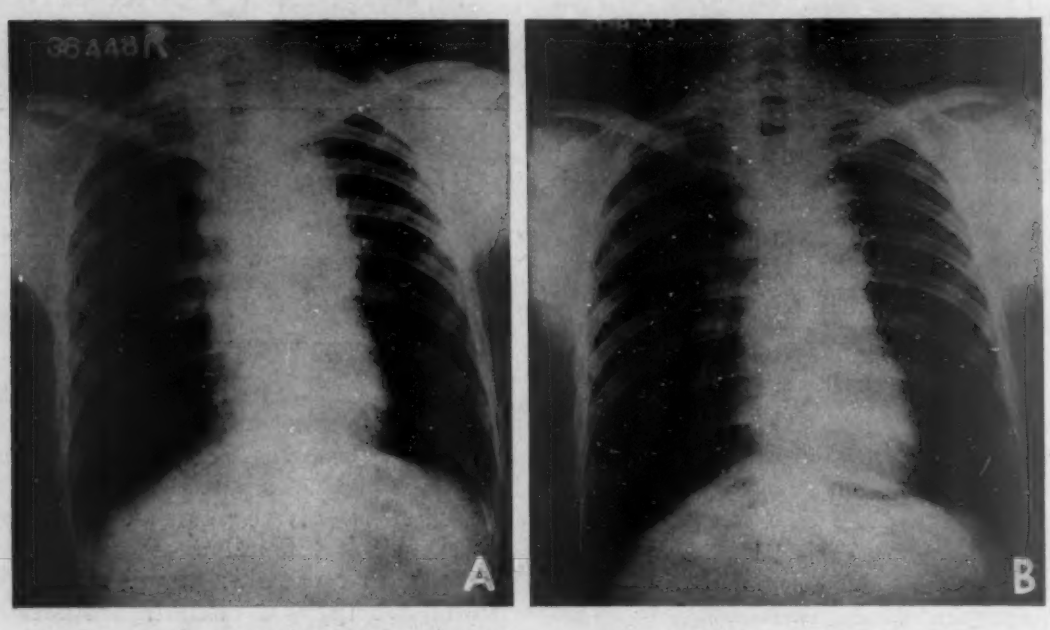

FIG. 1. Case 1. Hodgkin's disease. *A*, massive enlargement of mediastinal and hilar lymph nodes in a veteran, aged twenty-seven, associated with superior vena cava compression, fever, marked weakness, too ill for transport to Radiotherapy Department. *B*, After nitrogen mustard therapy, there is considerable regression in hilar and mediastinal lymph nodes associated with excellent clinical response lasting four months.

Of the 13 cases considered suitable for a second course, 61 per cent responded favorably, compared with 85 per cent remissions following the first course (Table II).

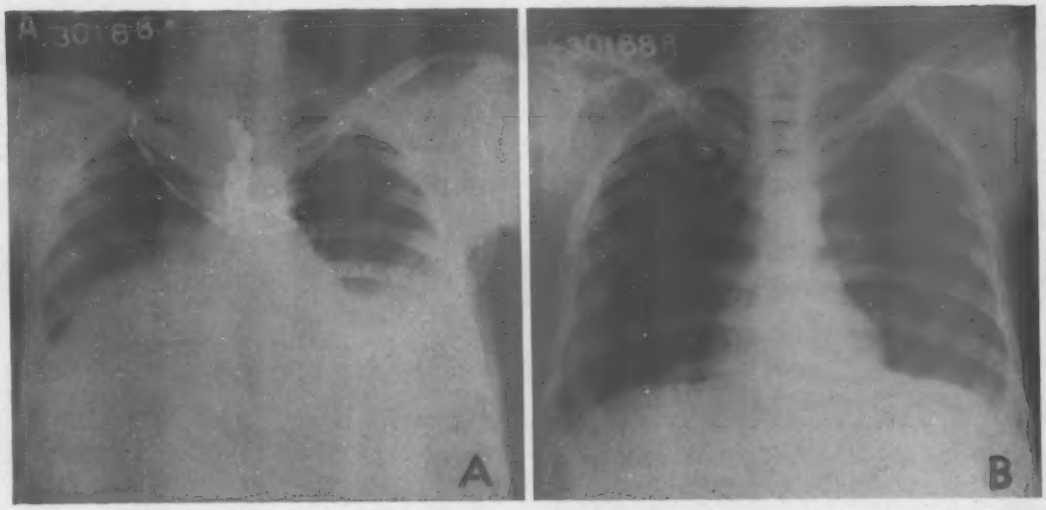

FIG. 2. Case II. Hodgkin's disease. *A*, December 16, 1947. Pericardial and bilateral pleural effusions. White male veteran, aged twenty-four, radioresistant. Associated with high fever, marked dyspnea, edema of lower extremities, splenomegaly. *B*, February 11, 1948. Regression of effusions thirty-five days after HN_2 therapy with complete relief of constitutional symptoms and dyspnea and regression of edema and splenomegaly.

A limited clinical study of this kind does not lend itself easily to statistical analysis; especially is this so because of the small number of cases of each disease entity. It is our clinical impression that the majority of the treated Hodgkin's disease patients,

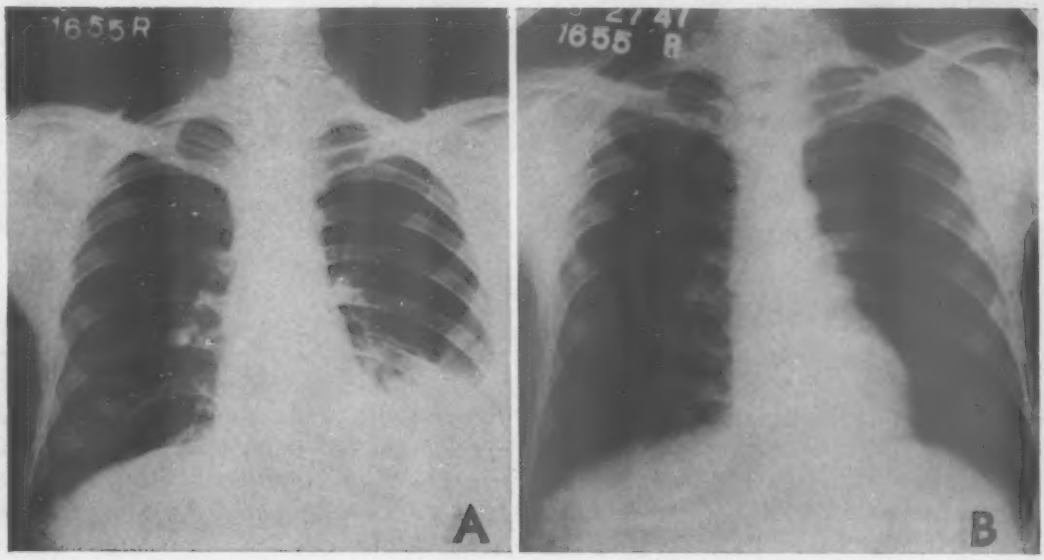

FIG. 3. Case III. Hodgkin's disease. *A*, March 12, 1947. Left basal infiltrate, pleural effusion and segmental atelectasis in white male veteran, aged twenty-five, with Hodgkin's disease of four and a half years' duration, now radioresistant, and generalized with severe constitutional symptoms, hepatosplenomegaly and involvement of retroperitoneal nodes. *B*, March 27, 1947. Complete regression of pulmonary involvement ten days after completion of nitrogen mustard therapy, associated with disappearance of constitutional symptoms. Remission of four weeks.

otherwise hopeless, enjoyed a relatively brief, but comfortable prolongation of life measured in weeks or months.

Lymphosarcoma. Of the 6 cases of lymphosarcoma, 2 had a favorable remission lasting 19 days and 145 days respectively—no benefit resulted in the 1 case of giant follicular lymphadenopathy. Of the 4 reticulum cell sarcomas, 2 benefited for intervals of seven and eighty-two days respectively. One of these patients (Fig. 4) had a large foul pendulous mass in the right axilla resistant to radiotherapy. After a single course of HN2 this lesion regressed and the patient was generally improved, for a period of nearly twelve weeks.

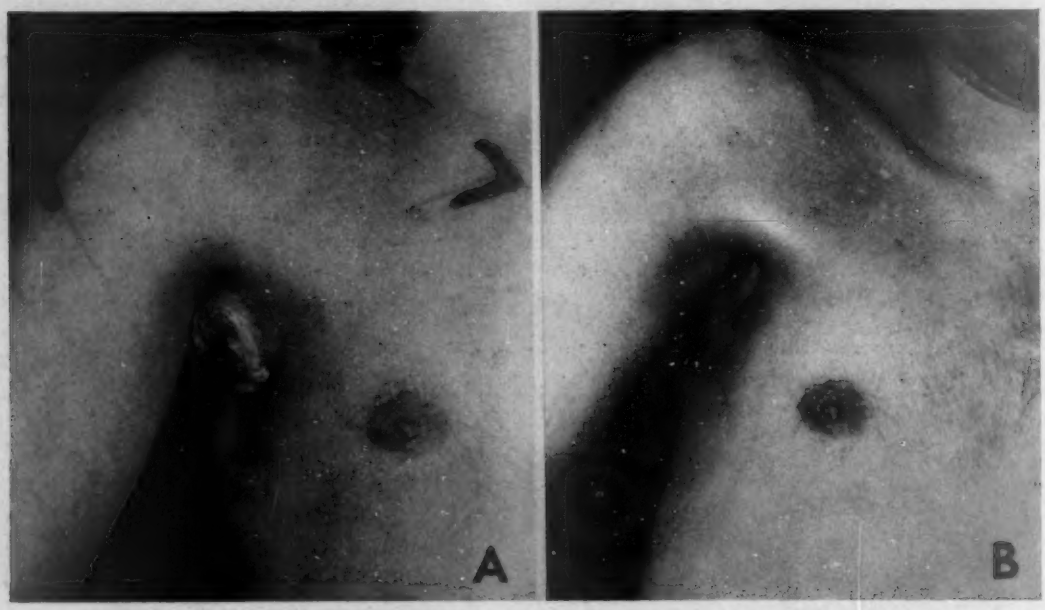

FIG. 4. Case IV. Reticulum cell sarcoma. *A*, fungating tumor in right axilla, previously resected and heavily irradiated, now radioresistant. Associated with generalized malignant disease. *B*, regression of tumor thirty days following HN2 therapy. This remission lasted eighty-two days and was associated with general improvement in clinical status.

Leukemia. Of the 6 cases of chronic leukemia, 2 improved for intervals of less than one week. These brief remissions were accompanied by a drop in leukocyte count with reduction in lymph node enlargement and regression of splenomegaly. These cases were far advanced and generally radioresistant.

Others[5,7] have reported somewhat better results in a larger series of cases. In the acute leukemias, all investigators agree, the same discouraging results are obtained from HN2 therapy as from other agents. To this group we add our single case.

Mycosis Fungoides. One of the 2 cases of mycosis fungoides responded briefly with moderate regression of lesions and relief from intractable, generalized pruritus. This patient enjoyed a remission of three weeks after which his condition became rapidly retrogressive.

Miscellaneous Malignancies. There were 18 cases of miscellaneous malignant tumors —far advanced and inoperable (Table 1). None derived any appreciable benefit from HN2 therapy and may be dropped from further consideration. It is important to note that no evidence of histopathological change has been found in epithelial cancers following nitrogen mustard therapy, regardless of dosage.[14]

Bronchogenic Carcinoma. In the Radiation Clinic more than 6,000 cases of inoperable bronchogenic carcinoma have received pal-

liative deep roentgen therapy in the past fifteen years. We are convinced from this experience that judiciously administered radiation has much to offer these patients in terms of relief from pain, hemorrhage, intractable cough, dyspnea, and even clearing of atelectasis and obstructive pneumonitis.

Since January, 1947, those cases of inoperable bronchogenic carcinoma which proved to be radioresistant, with advanced pulmonary infiltrations and compression of the superior vena cava, have received HN2 therapy. Of 16 cases so treated, 9 had a favorable remission lasting an average of twenty-seven days and sometimes as long as ten weeks. These patients were relieved of intractable cough, dyspnea and pain with concomitant improvement in appetite, weight and strength. There was roentgenological evidence of regression of atelectasis (Fig. 5); disappearance of obstructive pneumonitis (Fig. 6), and relief from superior vena cava compression (Fig. 7). Results were equally good in anaplastic and in well differentiated lesions. Of 7 cases with severe compression of the superior vena cava, 3 responded favorably. In such cases we would prefer HN2 rather than radiation therapy in order to obtain a far more rapid response and to obviate the danger of sudden edema and mediastinal strangulation which may follow irradiation. Although no evidence of histopathological changes have been found[14] in bronchogenic carcinoma treated with HN2, the clinical benefits are indeed gratifying. It is possible that these benefits may be the result of the influence of HN2 on the tissue reaction around the bronchogenic tumor but not actually in it.

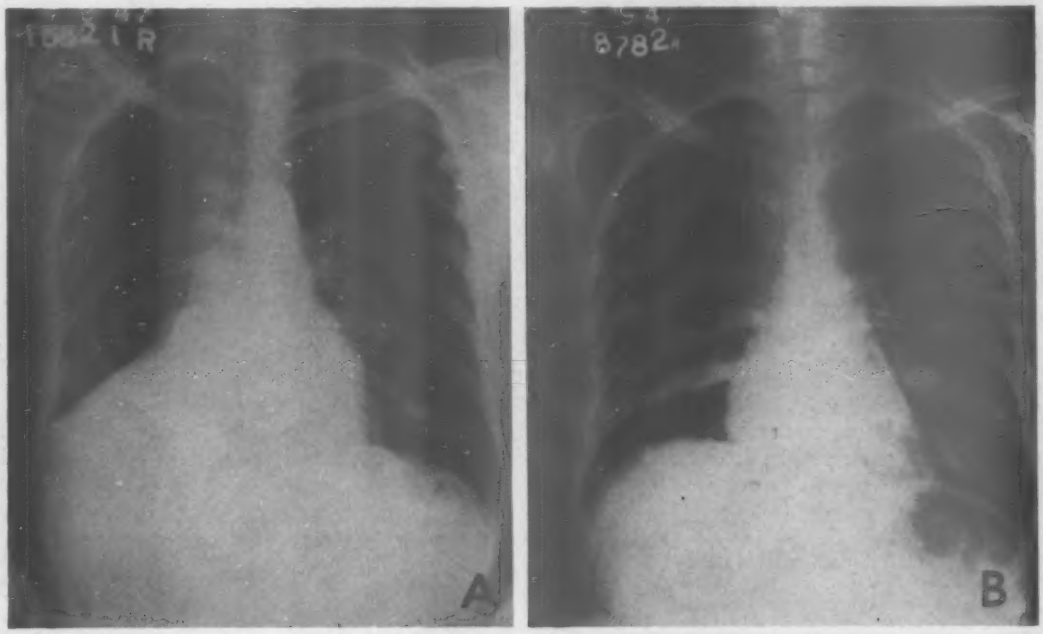

Fig. 5. Case v. Bronchogenic carcinoma. *A*, April 9, 1947. Atelectasis right lower lobe in a veteran, aged forty, with metastatic deposits in both lung fields and in the mediastinal nodes, associated with marked dyspnea, pain, fever, chills, and anorexia. Too ill for transportation to Radiotherapy Department. *B*, May 19, 1947. After HN2 therapy, regression of atelectasis, right lower lobe, associated with remarkable clinical improvement, improvement in appetite, strength and relief from fever and dyspnea. However, note enlargement of metastatic parenchymal deposits.

SUMMARY AND CONCLUSIONS

1. The determination of the role of nitrogen mustard (HN2) in the treatment of malignant disease is as yet in the investigative phase. Nevertheless, in these pre-

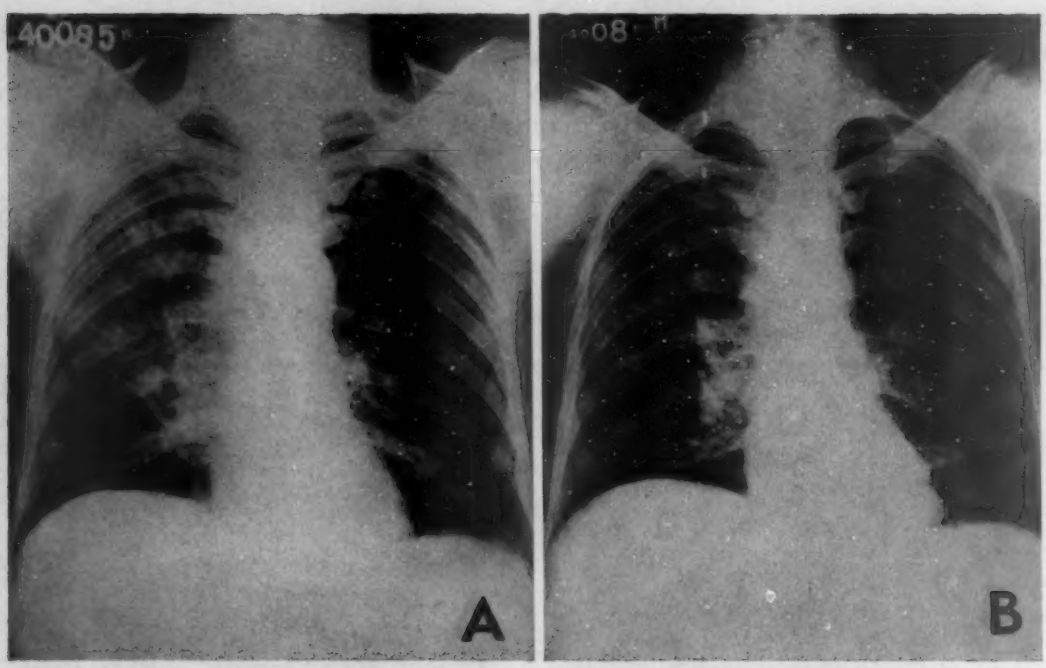

FIG. 6. Case VI. Bronchogenic carcinoma. *A*, May 10, 1948. Obstructive pneumonitis, right upper lobe, with mediastinal and hilar lymphadenopathy in a veteran, aged forty-nine. Associated with superior vena cava compression and massive hepatosplenomegaly. Patient extremely ill and too weak for transportation to Radiotherapy Department. *B*, June 18, 1948. One month after nitrogen mustard therapy. Note clearing of obstructive pneumonitis, diminution in lymph node involvement, associated with striking clinical improvement.

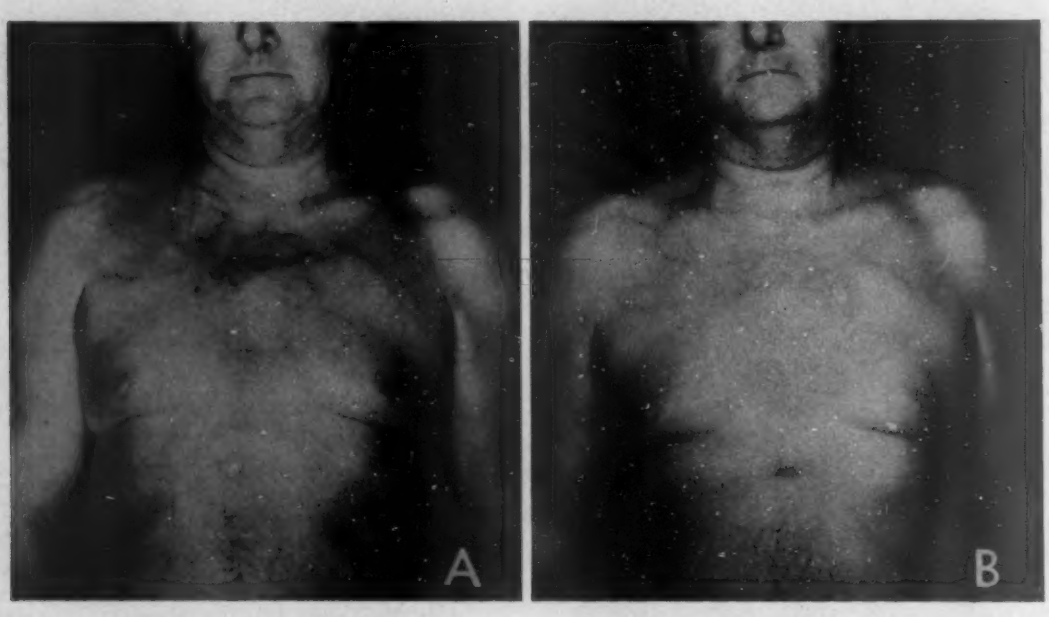

FIG. 7. Case VII. Bronchogenic carcinoma. *A*, infra-red photograph of fifty-five year old veteran with severe compression of superior vena cava by tumor mass. Note enormously dilated venous channels in chest wall. *B*, ten days after nitrogen mustard therapy infra-red photograph reveals regression of dilated venous channels, associated with striking symptomatic benefit, lasting one month.

liminary studies there has become apparent a pattern of behavior that merits presentation and discussion.

2. It is already clear that HN2 is not a *cure* for any malignant disease. Its effect is purely palliative and this effect may be principally observed in the malignant lymphomas. HN2 should not be employed in *early localized* Hodgkin's disease or lymphosarcoma. In these patients the best chance for survival is in rigorous local roentgen therapy. Hare, Mulry and Sornberger[6] have reported a five year survival of 39 per cent in patients irradiated for early localized lymphoid tumors.

3. It is our opinion that HN2 is not a *substitute* for roentgen irradiation in early *generalized* malignant lymphomas, when they remain responsive to roentgen therapy. Our control experience in the radiation treatment of more than seven hundred such cases supports this conclusion. Such patients may survive for several years after being treated with carefully planned, fractionated radiation therapy. Local roentgen therapy causes far less injury to the bone marrow than the systemic effect of nitrogen mustard. In addition, the testes may be quite adequately shielded during irradiation, while in nitrogen mustard therapy they are entirely vulnerable. Radioresistance is not encountered in these diseases until the malignant process is advanced. It is at this time that HN2 therapy is justified and of aid in the treatment.

4. We do not support the suggestion that this drug be employed as *maintenance* therapy in malignant lymphomas, including the chronic leukemias. The cumulative systemic intoxication thus induced leads to a hypoplastic or aplastic bone marrow and atrophy of the testes. The leukopenia, anemia and thrombocytopenia induced at an early stage in these diseases by nitrogen mustard may contraindicate the use of irradiation at a later period when the latter may be much needed.

5. We believe that the therapeutic radiologist will find in HN2 an indispensable systemic adjunct in the treatment of advanced, generalized malignant lymphomas at intervals when irradiation becomes ineffective or unfeasible. Nitrogen mustard is of aid in the treatment of inoperable bronchogenic carcinoma. In other malignant disorders HN2 is apparently ineffective.

It is to be earnestly hoped that in the near future other congoners of the nitrogen mustards will be found which will be much less toxic and far more effective.

The authors wish to express their deep appreciation for the unstinted cooperation of their colleagues in the Medical and Radiological Services. We are indeed grateful to Mrs. Marcia Taterka for her generous aid in preparing the manuscript. To the Medical Illustration Department we extend our thanks for the excellence of the photographic material.

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DISCUSSION

DR. TRAIAN LEUCUTIA, Detroit, Mich. The subject so ably presented by Dr. Roswit is very timely, since various types of chemotherapy used either alone or as adjuncts to radiation therapy are receiving considerable attention today. As Dr. Roswit hinted, there is a tendency to indiscriminate use and, especially in a group of compounds as toxic as the nitrogen mustards, not infrequently a very perilous situation might arise.

I was greatly impressed by the two late effects mentioned by Dr. Roswit, the effects on the hematopoietic and on the generative systems. It appears that the ordinary dosage injures the organs only temporarily, and that complete regeneration follows. Evidence is now accumulating, however, to the effect that the damage to the cells of the reproductive system, even with such a small dose as indicated here, may become permanent.

Considering that the patients of the lymphomatous group and especially those affected with Hodgkin's disease are young, and since roentgen therapy with the now more or less standardized technique leads not infrequently to satisfactory results, great care must be exercised in selection of the cases for nitrogen mustard gas therapy.

I thoroughly agree with Dr. Roswit that, for the time being, this treatment should be reserved only for the advanced cases and those unresponsive to other types of therapy.

At Harper Hospital, a group of 68 cases were treated, mostly of the lymphomatous type, and bronchogenic carcinoma, and the results paralleled those of Dr. Roswit in a very remarkable manner, so that one can say that at the present time, palliation is the most important part of the result.

There is an almost indefinite variety of nitrogen mustards which may be prepared exhibiting different forms and degrees of selectivity of action. It is possible that a better therapeutic agent may eventually be discovered. Therefore, we are justified in continuing with the trial of such compounds. The work of Dr. Roswit represents a very notable contribution in this respect.

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STUDIES ON RESPIRATORY MECHANICS

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I. HORIZONTAL BIPARTITION OF THE THORACIC CAGE (THE "THORACIC WAIST")

THE basic phenomenon of the mechanics of breathing is the expansion of the rib cage in the three dimensions of the space. Dilatation of the thoracic cavity is brought about by excentric movements of the ribs in all mammals; with regard to man's erect posture it is usually called *horizontal. Vertical* increase in volume is caused, essentially, by the inspiratory descent of the diaphragm. In lower vertebrates with highly developed pulmonary breathing, as in birds, the diaphragm is nonexistent. The role the diaphragm plays in the enlargement of the thorax may justly be regarded as secondary or as an addition to costal expansion as stated by Keith. Thus the fundamental principle of chest expansion consists in the rib movements. Rotation of the ribs is based on some simple mechanical laws that are easily recognizable in certain lower vertebrates who do not possess pulmonary breathing, e.g. reptiles. This original form of the enlargement of the visceral cavity is maintained—as we shall see—during the whole course of phylogenetical evolution up to the highest mammals.

Reviewing the literature, it becomes evident that the role of the muscular forces of thoracic dilatation in man is a very controversial problem. The action of the intercostales on the ribs has been disputed since Galen's time (the diversity of opinions have been enumerated in a paper by Polgar and Lendvai). Authors disagree concerning the action of the diaphragm, particularly on the ribs, the action of the levatores costarum, also whether the scaleni participate in the expansion of the thorax during quiet ordinary breathing. To approach these problems thorough study of the rib movements is an essential preliminary. This is attempted in the treatise which follows by two methods of investigation, viz. roentgenological observations and comparative anatomical studies.

The usual frontal roentgenogram of the chest very often displays a peculiar deformity of the osseous parts. It is most conspicuous in cases of augmented thoracic volume and consists in a bilateral, more or less shallow impression of the lateral chest wall. The greatest depth of this furrow (or sulcus) is found, as a rule, at the level of the sixth or seventh pair of ribs. The concavity appears as a constriction, like the waist of the body, and passes gradually into the marked outward convexity of the osteothorax. Its freqency increases with increasing age; and its greatest depth, reaching as far as about 2 cm., can be observed in old people suffering from chronic emphysema (Fig. 1). Smaller degrees of this furrow can be seen in numerous cases of increased thoracic volume (Fig. 2), and the deformity represents a valuable diagnostic sign of emphysema (not mentioned, however, in textbooks as far as I know).

Differences in the courses of upper and lower ribs in emphysema have been noted by Loeschke. He found the ventral parts of the *six upper ribs* of the emphysematic mostly bent upward and fixed in an "inspiratory" position, whereas the anterior parts of the seventh, eighth, ninth and tenth ribs were distinctly bent downward and occupied an "expiratory" position. He found this difference in the normal as well. To comprehend, however, the differences between the structure of the upper and lower halves of the rib cage as well as the significance of these differences with regard to respiratory mechanics, we have first to point out some structural peculiarities of the entire thoracic cage.

The impression of the lateral chest wall

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FIG. 1. A case of severe emphysema in a female, aged sixty-one. The thoracic volume is increased, the diaphragm low and stretched out; the lung fields are extraradiolucent. Note the deep lateral impression of the chest wall in the middle of the rib-cage causing a "double-balloon" form of the thorax.

is a common roentgen finding in cases of increased thoracic volume. Inspection of the normal osteothorax, however, shows

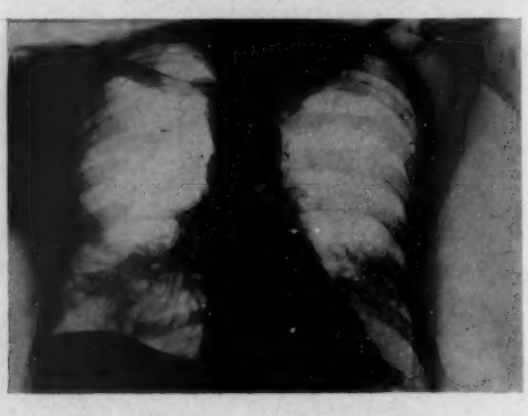

FIG. 2. "Thoracic waist" of moderate depth in a case of chronic alveolar emphysema. The volume of the superior hemithorax is particularly increased. (Sequelae of pneumopleurisy can be seen in the right lower lung field.)

that the constriction of the cavity at a fixed level is no accidentally arising pathological deformity, but a constant—though less conspicuous—feature of the normal skeleton (Fig. 3). It is a boundary between *two differently expanding parts* of the chest and at the same time the metameric segment where the periodical—or respiratory

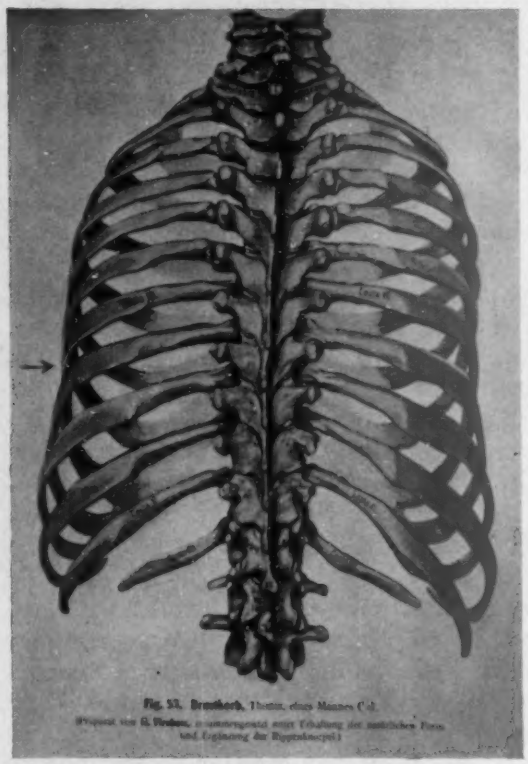

FIG. 3. Dorsal view of the normal rib-cage. The arrow indicates the lateral thoracic furrow. The necks of the ribs are hidden from view by the transverse processes in the upper hemithorax, they elevate above the transverse processes in the lower chest half. Note the gradual shortening of the transverse processes from above to below. (From Toldt.)

—as well as the permanent—or emphysematic—horizontal augmentation of the chest volume is the least. Therefore, it will be called in the following *thoracic waist* or *lateral thoracic furrow* (sulcus thoracis lateralis).

Concerning the attachments of the ribs to other bony elements, the structural

difference between upper and lower ribs is shown in front by the presence of the five false ribs 8–12. Because the eighth, ninth and tenth ribs have their cartilages attached to the cartilage of the rib above, their anterior ends can readily move away from the midline in a mere lateral direction (without any elevation of the rib). This kind of horizontal thoracic enlargement has been termed *flank respiration;* it is predominant in quadrupeds, but easily demonstrable in special circumstances also in the human (see below).

From a mechanical point of view more important structural differences between upper and lower halves of the chest can be found on the dorsal aspect of the osteothorax (Fig. 3). Most conspicuously the horizontal situation of the rib necks and their congruency to the level of the transverse processes changes as we proceed from above downwards*: (a) ribs and transverse processes are situated at the same level in the six upper segments; the rib neck is thus hidden behind the process in the dorsal view, (b) the neck of the seventh rib peeps a little above the process, and (c) in the next five segments each rib appears in its full breadth *above* the transverse process.

Corresponding to the upward shift of the ribs the vertebral and costal facets of the costotransverse articulations become displaced: they migrate respectively from the anterior surface of the transverse processes upon their superior (cranial) wall and from the dorsal surface of the ribs upon their inferior (caudal) margin (Fig. 5, 6 and 8). Transverse processes of the upper six vertebrae are flattened anteroposteriorly, those of the lower six are gradually shortening prisms. Whereas in the upper six joints the articular space runs approximately in the frontal plane, that of the lower ribs runs approximately horizontally (with some sloping forwards and sideways. Fig. 4–8). The incongruency of rib necks and transverse processes as well as the displacement of the costotransverse joints corresponds to the cephalocaudally progressive declination of the transverse processes (Fig. 4 and 5). In the upper vertebrae

Fig. 4. Articular facets of the thoracic transverse processes from the third to the tenth (outlined in india ink). The superior facets are distinctly excavated and directed anterolaterally. The lower facets decrease in size, flatten and migrate upon the anterosuperior wall of the prismatic transverse process. The interval between two subsequent transverse processes increases cephalocaudally.

the right and left processes form an obtuse angle opening *superiorly*. Figures 3 and 5 show that this angle straightens to 180° in the sixth or seventh vertebra and changes to an angle opening *inferiorly* in the eighth,

* Some minute details of the following analysis are much more easily comprehensible with the concurrent inspection of the skeleton.

ninth and tenth (eleventh and twelfth being rudimentary). Owing to the caudal declination of the transverse processes the distance between two subsequent processes

FIG. 5. Roentgenogram of a human skeleton. Left costotransverse articular surfaces coated with contrast substance. Concavoconvex joints in the upper, small parallel gliding surfaces in the lower hemithorax. Note shortening and progressive decline of transverse processes and gradual approach of costotransverse joints to the spine from above to below.

gradually increases from top to bottom. In the lower chest half there results a free interval in which the rib neck can glide *backward* on the plane articular facet of the transverse process. This movement is characteristic only of the respiratory shift of the ribs 7–11, and will be demonstrated below; it secures transverse enlargement of the lower hemithorax by means of flank respiration or, as it should be called, by *abduction* of the lower ribs. It is a rotation around a vertical axis with a concurrent dorsal displacement or *repulsion* of the rib neck (Fig. 10 and 17).

Further differences between upper and lower hemithorax concern the situation and form of the costotransverse articulations. Examination in detail shows the following changes when proceeding from above downwards:

(1) Costotransverse articulations gradually approach the midline (Fig. 3–5). This is due to three causes: (a) the length of the transverse process diminishes cephalocaudally (Fig. 3) so as to become but small tubercles in D11 and D12 (so-called transverse tubercle); (b) the long axis of the process runs almost frontally in the upper vertebrae, but declines backward more and more in the lower vertebrae. Owing to this, the tip of the process comes nearer to the median line. The first pair of processes form an anteriorly open angle of 140° and the tenth pair are almost parallel to each other; (c) the articular facet shifts a little toward the vertebral pedicles on the surface of the lower processes.

Mechanically these differences signify that the nearer the costotransverse joint to the pivot of the rib movement, i.e. to the costovertebral articulation, the less its limitative and breaking action on the rotation of the rib head. Accordingly, this fact that the costotransverse joints come progressively closer to the midline from above downwards plays an important part in the more ample lateral movement (abduction) of the lower ribs.

(2) As to the form of the costotransverse joints, their facets gradually decrease in size. They occupy the whole breadth of the ventral surface of the six upper processes, but decrease so much that the size of the tenth is less than half of any of the six superior ones (Fig. 4). The articular facet is nondeveloped in the eleventh, twelfth, sometimes in the tenth and exceptionally in the ninth vertebrae (as shown below).

Concurrently therewith, the depression of the vertebral facet disappears. These joints of the upper six vertebrae are concavoconvex, i.e. the rib carries a roundish head and the transverse process an excavated fovea (Fig. 4–6). The transverse processes of the seventh, eighth, ninth and tenth vertebrae, however, do not possess any fovea; these joints are built of flattened, plane and parallel gliding surfaces, like the intervertebral articulations. These changes, in accordance with the shift of the joint from the anterior surface of the process upon its cranial surface, provide for repulsion by making possible the small but distinct backward inspiratory movement of the neck of the ribs 7–11. The characteristic diminution and change of the costovertebral joint from a condyloid joint to an arthrodia (gliding joint) is best seen in the roentgenogram (Fig. 6).

Based upon the enumerated constructive differences, the rib cage is to be divided into an upper and lower half characterized by the following:

Superior hemithorax	Inferior hemithorax
The transverse process	
Long and flat	Short and prismatic
Longer axis frontal	Nearly sagittal
Level in horizontal congruency with the rib neck	Shifting beneath the rib neck
Angle of right and left processes opening upwards	Angle 180° or opening downwards
The costotransverse joints	
As large as the whole breadth of the transverse process	Decreasing to half the size
Composed of spheroid head and excavated fovea	Facets are flat parallel gliding surfaces
On the distal end of the process	Nearer to the vertebral pedicles
Articular cavity approximately in the frontal plane	Articular cleft approximately in the horizontal plane

This horizontal bipartition of the human osteothorax is of the utmost significance as to the mechanism of the rib movements. It is, therefore, a division not only from an anatomical but also from a functional point

Fig. 6. Roentgenogram of the thoracic spine of a healthy male. Concavoconvex, ginglymoid costotransverse joints, indicated by black arrows, in the upper hemithorax. Slit-like articular spaces with parallel gliding facets, indicated by white arrows, in the inferior hemithorax.

of view and marked on the chest contours by the lateral thoracic furrow.

As far as I could find out, Aschoff is the only author who makes mention of the typical impression of the side walls of the chest at its medium height. Quoting the

findings of Loeschke, he considers the different course of the upper and lower ribs as an expression of the inspiratory *elevation* of the cranial part of the thorax and the *enlargement* of the caudal part respectively. Apart from this, he points out the fact that the intercostal spaces are always the narrowest near the sixth or seventh rib and enlarge from here up- and downwards. "*Gleichzeitig besteht hier eine deutliche Abflachung der seitlichen Brustwand.*" (At the same time there exists here a marked flattening of the lateral chest wall.)

II. PHYLOGENESIS OF THE RIB JUNCTIONS

Comparative morphology is the essential science, not to say the only road to the knowledge of life.—Gegenbaur

To comprehend the intricate mechanism of the rib movements in man one has to start from the simple anatomical conditions as present in some lower vertebrates.

The ribs are ventral excrescences of the vertebrae; their primary mechanical function consists in carrying the weight of the common body cavity, the celom. In most species of vertebrates they are fastened to the vertebrae at two points, the lateral called diapophysis and the medial parapophysis. This original or *two-headed* attachment regresses, however, in some forms, and the rib becomes attached to the vertebra at one point only, a so-called *one-headed* rib. The heavier the weight of the celom and the greater the requirements to the firmness of the rib junctions the more obligatory the two-headed attachment of the rib. Thus we find two-headed ribs first and foremost on the upper vertebrae near the skull, where the ribs have to serve as firm bases for the action of the upper limbs and for their musculature. Proceeding caudally, the attachments become less strong, and one-headed junctions may appear, as in the eleventh and twelfth ribs of man. This difference in strength of connection of upper and lower ribs to the vertebral column is of great importance for the understanding of the breathing movement; as we shall see, it is one of the essential causes of the difference between the respiratory movement of the upper and lower hemithorax.

Originally both costovertebral joints were placed on the transverse process. In the course of phylogenesis the medial articular facet, the parapophysis, migrated either to the vertebral body (e.g. snakes or first, eleventh and twelfth human ribs) or, separated into two parts, to the adjacent margins of two subsequent vertebrae as an "intervertebral parapophysis." This latter way of migration explains the mobile intervertebral attachment of the rib head opposite the intervertebral disc in most mammals. The tubercle of the rib, at the same time, maintained its contact with the transverse process.

The thoracic ribs remain two-headed in vertebrates whose ribs are constantly compelled to bear the weight of the celom (birds, quadrupeds, etc.). Owing to the excessive weight of its far protruding and erectly carried thorax, the strongest fastening of the rib to the spine is to be found in the gorilla. Four points of rib attachment are present in this animal (Fig. 13–14): the head joins two subsequent vertebral bodies and the costal tubercle—possessing two separated articular facets—two adjacent transverse processes.

Contrary to this, two-headed junctions become superfluous and disappear, as pointed out by Ihle, when either the trunk lies on the ground (e.g. snakes) or water supports the body weight (e.g. *Ichthyosauria*, *Cetacea*). There remain one-headed ribs acquiring thus a far greater mobility. Two different possibilities arise in this way: the ribs may be used either for locomotion as in snakes (see below) or for an excessively large dilatation of the thorax (by means of simple abduction) in order to inhale extraordinary large quantities of air as in *Cetacea*. This regression of two-headed rib junctions takes place in two different ways.

In the first way the capitulum fuses with the tuberculum, and the rib becomes

attached solely to the diapophysis. This occurs in *Cetacea*, in snakes, and sometimes also in the human skeleton, where most accessory lumbar ribs do not join the vertebral body and articulate merely with the tip of the transverse process.

The second way consists in the regression of the costotransverse articulation and the junction of the rib solely with the parapophysis. This kind of one-headedness is to be found in the lowest mammals (Fig. 16) and in the regressed eleventh and twelfth ribs of man. One-headed attachment of the tenth rib represents a frequent variation of the human spine (not mentioned in anatomical textbooks). In statistical evaluation of 210 roentgenograms of this region I found one-sided nondevelopment of the tenth costotransverse joint in 17 cases (8.5 per cent) and double-sided absence in 61 cases (30 per cent; see Fig. 7). Moreover, one-sided absence of the ninth joint was found in 3 cases (1.5 per cent; Fig. 8). Regressive one-headedness starts in the caudal parts of the thoracic cage and proceeds cranialward. The function of the transverse processes as *supports and buttresses of the ribs* acts in parallel with this change; it is characteristic of the human skeleton that the transverse processes of the lowest thoracic vertebrae are much shorter than those of the upper or reduced even to small transverse tubercles (Fig. 3). All these regressive changes, in addition to the above mentioned decrease in size and the medial shift of the costotransverse joints, provide for a greater mobility of the lower ribs and enable them to bring about horizontal enlargement by means of rotation around the vertical axis (abduction).

In the whole animal kingdom the movements of the ribs are governed by the costovertebral articulations; and the study of the latter reveals a general principle

Fig. 7. Bilateral nondevelopment of the tenth costotransverse articulations; one-headed tenth ribs.

Fig. 8. Bilateral nondevelopment of the tenth and unilateral absence of the ninth costotransverse joints (black arrows). Note the flat gliding surfaces of the costotransverse articular facets (white arrows).

Fig. 9. Vertebral end of a rib and one vertebra of the boa constrictor (*Python reticulatus*). The costovertebral articular facets show clearly the configuration of a saddle joint. (Specimen of the National Museum in Budapest. Courtesy of Baroness B. Fejérvary.)

explaining the mechanism of respiratory rib excursions. Owing to the complicated structure of the human thorax and the secondary ventral declination of the ribs due to man's erect posture, one has to cope with great difficulties in studying the breathing movements in man. Therefore our investigations have to start from more simple conditions as present in *Reptilia*. The rib junctions of snakes have served as a starting point in this study.

The ribs of snakes are uniform, flattened cephalocaudally and curved only in one plane; they are "false" ribs, like the two lowest in man, and thus disconnected in front. Each pair of ribs forms an apparatus like the arms of a pincer or the arms of a compass. Costotransverse joints are nonexistent, and the rib joins the vertebra in a simple way. Figure 9 shows one vertebra and the vertebral part of a rib of the boa constrictor (*Python reticulatus*). As seen,

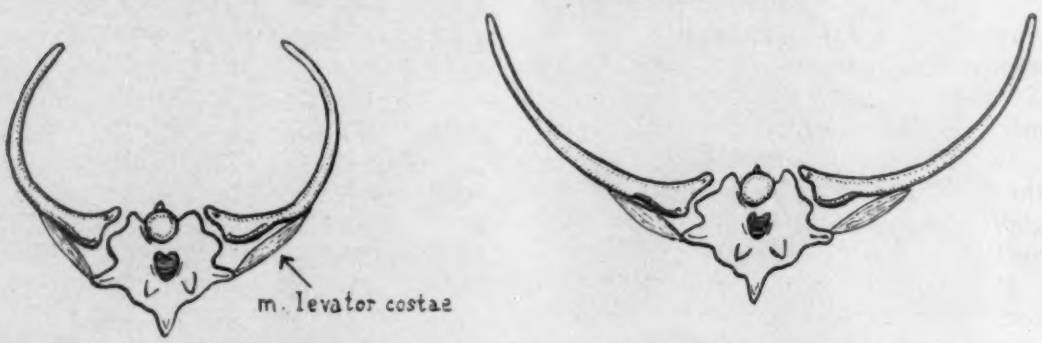

Fig. 10. Diagram showing abduction of the ribs of a snake. Backward displacement (repulsion) of the costal manubria due to the contraction of the levatores. (Modified after Sibson.)

the costovertebral articulation of this animal is the best example of a *saddle joint*. The oval head belongs to the vertebral body and is divided into two demi-facets by means of a small *bony crest*. The glenoid cavity is placed on the rib head and shows a shallow depression separated likewise into two parts. The articular space forms an angle of 45° between the frontal and sagittal plane (Fig. 12).

According to the general rule of saddle articulations the rib can move like a one-armed lever around *two axes:*

(1) *Abduction* (Fig. 10) is brought about by the rotation of the articular end of the rib around a *vertical* axis, whereby the rib head glides along the longitudinal diameter of the articular surface. Consequently the

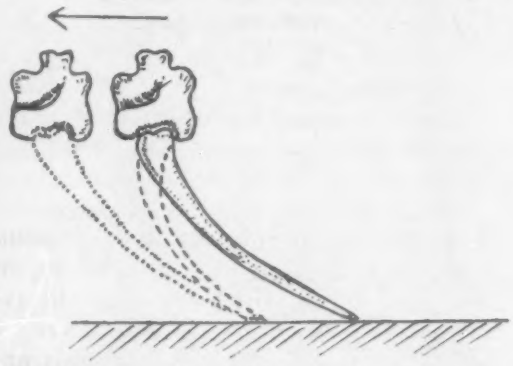

Fig. 11. Elevation of the rib of a snake. The contraction of the levator elevates the rib from the starting position into the curved position (indicated by dotted line). With the muscle relaxing the rib stretches itself (punctuated line) and thus pushes the vertebra forward. (Redrawn after Wiedemann, 1932.)

rib portions near the fulcrum shift backward approaching the spinous process. This shift is called *repulsion* ("Rückstoss") in the mechanics of rib excursions.

(2) *Elevation* (Fig. 11) takes place when the rib rotates on a *horizontal* axis, the head gliding along the short diameter of the vertebral surface.

It is easy to convey a clear idea of both components of this basic *biaxial* movement:

Abduction separates right and left ribs from one another like the opening of a pincer and dilates the body cavity perpendicularly to the vertical axis of the body (Fig. 10). Since anterior connections of the ribs are nonexistent, the animal may thus

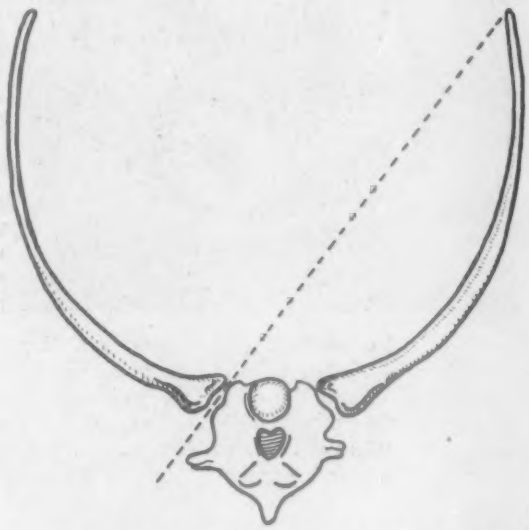

Fig. 12. The axis of elevation of the rib of a snake (dotted line) connects the costovertebral joint with the point of the contralateral rib.

devour a bit greater than the diameters of its trunk. The axis of this dilatation coincides with the short vertical diameter of the rib joint, i.e. with the long axis of the trunk.

Elevation lifts the anterior ends of the pair of ribs cranialwards and may accomplish thereby locomotive function: the snake "walks on its ribs" (Fig. 11). The rotatory axis coincides with the longer diameter of the articular surface and runs transversely (perpendicularly to the long axis of the body) and obliquely from the fulcrum toward the anterior end of the opposite rib (Fig. 12).

Both abduction and elevation are brought about in the snake by the levatores costarum (Fig. 10). Each of these muscles arises from the transverse tubercle of the vertebra above and running obliquely downwards and sideways is inserted on the paravertebral part of the rib. The combination of both basic movements results in the "*spinning*" *movement* of the

Fig. 13. Costovertebral articulations of a *Gorilla gorilla beringei*. The pointed head of the rib is received in a deep wedge-shaped trough built by two subsequent vertebral bodies. Bipartition of the articular surface of the transverse process.

rib, similar to the circumduction of the thumb. The carpometacarpal joint of the thumb is the most perfect biaxial saddle joint of the human body, where circumduction of the metacarpus by synchronous rotation around two axes is allowed, axial rotation, however, around an axis coinciding with the long axis of the metacarpus, is prevented.

In the lowest classes of mammals conditions are similar to the simple mechanism discussed above. The skeleton of oviparous *Monotremata* shows a transitory form. So the ribs of the spiny anteater (*Echidna aculeata*) join two vertebrae with an intervertebral parapophysis, like those of higher mammals (Fig. 16); yet, according to Owen, Bolk and confirmed by my own investigations, the ribs are one-headed, and costotransverse articulations are missing, except sometimes the first and second thoracic segments. This is in accordance with the above mentioned rule that the upper ribs require a more firm attachment to the spine. In the class of *Marsupialia* I found—in a specimen of opossum (*Notoryctes typhlops*)—thick transverse processes carrying large masses of levator muscles, but no costotransverse joints.

Conditions in the higher classes of mammals are similar to those in man except that the bipartition of the rib head, this sign indicating the biaxial-condyloid construction of the costovertebral joint, is more strongly marked. Two-headed rib attach-

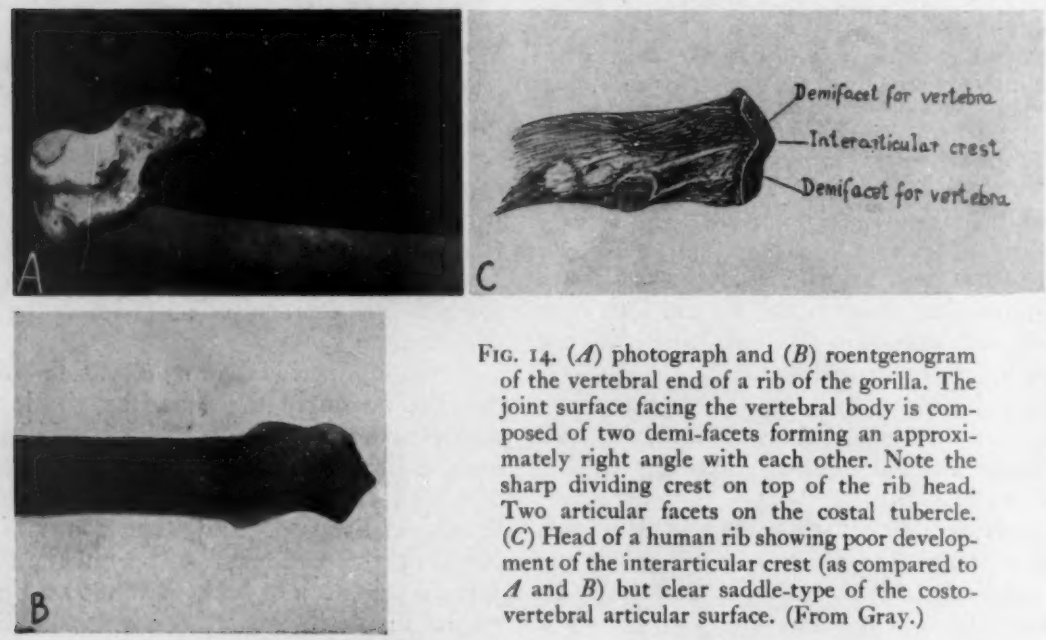

Fig. 14. (*A*) photograph and (*B*) roentgenogram of the vertebral end of a rib of the gorilla. The joint surface facing the vertebral body is composed of two demi-facets forming an approximately right angle with each other. Note the sharp dividing crest on top of the rib head. Two articular facets on the costal tubercle. (*C*) Head of a human rib showing poor development of the interarticular crest (as compared to *A* and *B*) but clear saddle-type of the costovertebral articular surface. (From Gray.)

ments are firm and massive in some mammals whose spine has to carry a heavy weight. Costovertebral articulations of the rhinoceros enclose rib-heads almost as bulky as the head of the human humerus. The basic biaxial type of movements, however, persists; it is revealed by the saddle construction with the dividing crest on the facet of the rib permitting circumduction but checking axial rotation. In some species the demi-facets of the rib head are separated by a shallow sulcus (e.g. deers).

As an excellent comparative anatomical object of study the rib junctions of the gorilla may elucidate the mechanism of rib excursions. In the family of orthograde primates, man's next akin yields the best example to demonstrate the basic biaxial principle of rib movements, this kernel of respiratory mechanics. Owing to the heavy weight of the gorilla's chest, as stated earlier, the major part of the rib attachments (DVI–DXIII) are very firm (Fig. 13 and 14): (*a*) The rib head is rostrally pointed and fitted into a deep wedge-shaped joint cavity distributed upon a pair of vertebral bodies. (*b*) The costal tubercles of the lower eight ribs possess *two* articular facets situated on the upper and lower margins; they articulate with the upper and the corresponding transverse processes respectively. The articular surfaces of the transverse processes are placed accordingly; the upper facet is inclined upward and the lower downward.

The bipartition of the rib head is much more definitely marked than that of the human rib head (Fig. 14). The articular surface is composed of two inclined demi-facets forming an approximately right angle with each other and separated by a thick and prominent crest. The saddle-like construction of the costovertebral joint is thus clear. The horizontal movement of the rib head in the trough-like excavation of the vertebrae, directed in the course of the crest, is self-evident and easily practicable. Such a medial shift of 1–2 mm. length (Fig. 15) removes the lateral convexity of the rib as far as 10–20 mm. from the midline and

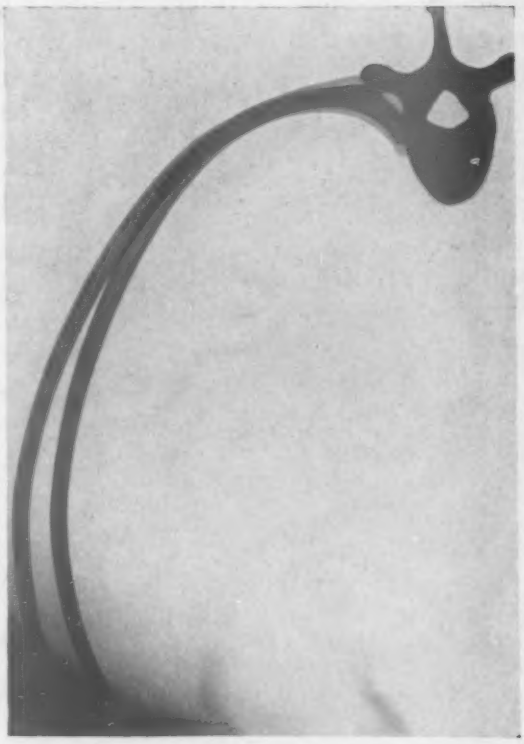

FIG. 15. Biphasic roentgenogram showing experimental abduction of a rib of the gorilla. Minimal horizontal shift of the head towards the vertebral body produces extensive transverse widening of the thoracic cavity.

enlarges the thoracic cavity horizontally by means of abduction. It differs from the abduction of the ribs of the snake or from that of the 7–11 human ribs, inasmuch as repulsion is checked by the firm attachments of the costal tubercle to *two* transverse processes. Despite this, abduction by rotation around a vertical axis is clearly recognizable. Elevation, on the other hand, can be readily performed and is promoted by the costotransverse gliding surfaces. Axial rotation (around the so-called "neck axis") is impracticable and checked by the sharp crest of the rib head.

In the course of these comparative anatomical studies a further important observation could be made. In a specimen of *Echidna* I found the following atavistic variation of the skeleton (Fig. 16):

In the right hemithorax there are ten ribs

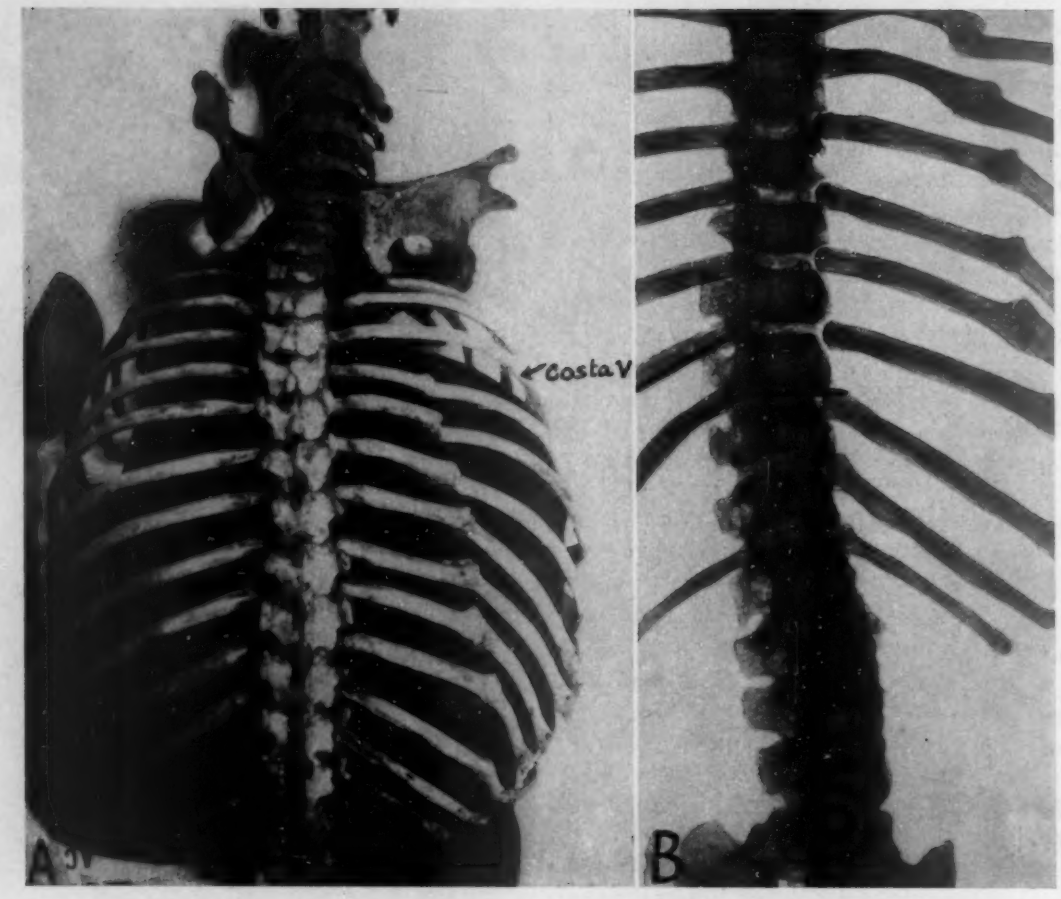

Fig. 16. (*A*) photograph and (*B*) roentgenogram of the dorsal rib wall of an *Echidna aculeata*. Most of the right-sided ribs show intercostal joints or synostoses at a downward increasing distance from the vertebral column. Residuals of the articular clefts are still visible (no fractures!). Compare this arrangement with the situation of the costal angles in man as seen in Figure 3. One-headed ribs.

(first, second and from the sixth to the thirteenth; the first two, however, not seen on the photograph) the dorsal segments of which are composed of two parts articulating with each other. These junctions are placed in an oblique line which gradually removes from the spine, analogously to the placement of the costal angles in man. They are imperfect joints step by step changing into synchondroses and synostoses. From the point of view of respiratory mechanics this transitory form, placed in the animal kingdom at the borderline between birds and mammals, permits a very interesting glance into Nature's laboratory. It yields valuable information as to the forces of respiratory rib movements for the following reason:

Ribs of lower vertebrates are mostly trior bipartite. In reptiles the *vertebrocostal*, *intercostal* and *sternocostal* portions are distinguished; birds possess a shorter vertebral and a longer sternal rib connected by a true joint with each other. Similar segmentation has been found also in some mammals, and the costal cartilage of man is regarded as analogous to the sternal rib. It follows from this that the above described specimen represents a hemilateral regression of the rib cage to more primitive conditions with separated vertebrocostal rib segments. Zoology teaches that the motive

power of the vertebrocostal segments as well as of the avian vertebral rib is the levator costae. The paravertebral part of the mammalian rib is analogous to this dorsal segment (as shown by the above observation); it reaches as far as the costal angle, where the rib turns forward. This portion is rough and tuberous and serves as a base of insertion for the levatores which hold and rotate the rib by this grip like a sword. This mechanism becomes evident when studying the pincer-like movement of the pair of ribs of the snake (Fig. 10). The contrast between the smooth axillary and the rough paravertebral portions of human ribs is still more conspicuous; it justifies the distinction of the part reaching as far as the costal angle as an anatomically and functionally separated segment of the rib and hence named *costal manubrium*. We may conclude therefore that the comparative morphological study of the above described mixed creature indicates how Nature used and transformed the forces present in lower vertebrates when passing to the changed and specialized respiratory apparatus of the mammal.

III. THE DILATATION OF THE HUMAN RIB CAGE

Taking as a basis the anatomical and functional horizontal bipartition of the human thorax as well as the results of the phylogenetic study of rib excursions, we may obtain a deeper insight into the respiratory dynamics of man.

Vertical increase of the chest volume is brought about essentially by the movements of the diaphragm (discussed in a previous paper of the writer). Horizontal increase results from the following components:

(1) *Widening* or lateral enlargement (*b* in Fig. 17) takes place as a result of the abduction (side-thrust, "Seitenstoss" after Felix) of the ribs.

(2) *Deepening* or sagittal enlargement is due to the addition of the propelling of the breastbone (propulsion, *a* in Fig. 17) and the dorsal displacement (repulsion, *c*) of the costal manubria. Propulsion or forward thrust ("Vorstoss") is a secondary movement caused by the elevation of the ribs, whereas repulsion is a direct effect of *extramural* muscle forces.

Widening cannot be examined in the living by roentgen projection from above (to wit, axially, as in Fig. 10 and 15). Further difficulties arise by the obliquity of the ribs in adults which produces intricate

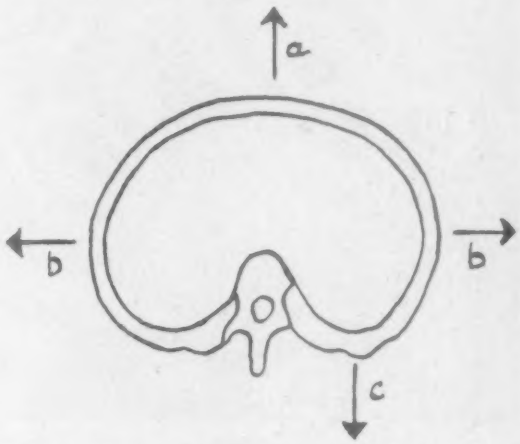

FIG. 17. Diagram illustrating horizontal dilatation of the chest. *a* = forward-thrust or propulsion; *b* = side-thrust or abduction; *c* = back-thrust or repulsion.

superimposition of shadows in the frontal roentgenogram. Therefore thoracic dilatation of the newborn should be chosen as a starting point, for the ribs run there almost as horizontally as in reptiles.

Figure 18 shows the inspiratory widening of a newborn's chest in the frontal view. The difference between the changes in form of the superior and inferior hemithorax is evident. The upper ribs become distinctly elevated on inspiration, whereas the horizontal lower pairs of ribs are widened transversely without any elevation. The side parts of the sixth, seventh and eighth ribs deviate from the midsagittal plane while abducted; so the dorsohorizontal rib segments elongate and the transverse thoracic diameter increases. Inspiratory enlargement of the intercostal spaces is unequal and fan-like and the greatest in

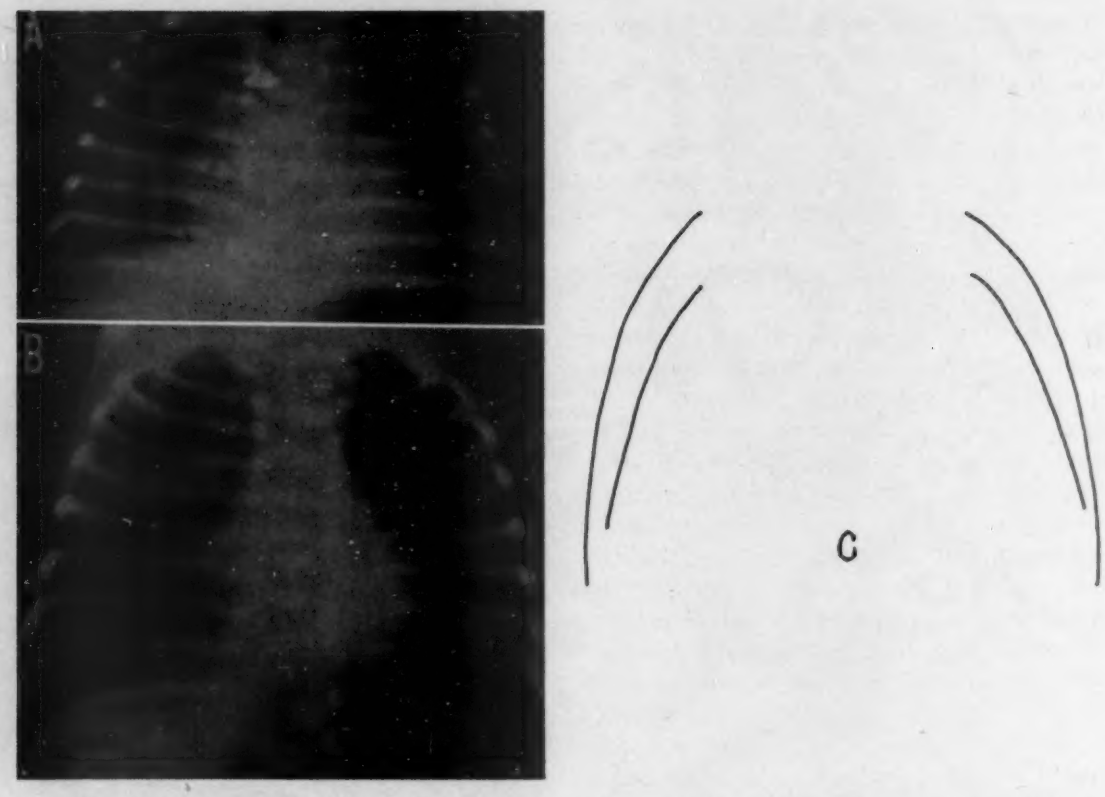

Fig. 18, *A, B, C.* Inspiratory dilatation of the thorax of a newborn as seen in the frontal roentgenogram. (*A*) expiration, (*B*) inspiration, (*C*) contour diagram of the expansion of the rib cage. Note bulging of the side walls on inspiration and fan-like enlargement of the intercostal spaces. (*A* and *B* from Caffey.)

the axillar parts. Side-to-side dilatation of the superior hemithorax appears apparently because each of the wider inferior pairs of ribs shifts upward in plane of the rib above.

The degree of abduction of the inferior ribs is unequal and the greatest in the eighth, ninth and tenth. Widening of the side-parts of the intercostal spaces and *bulging* of the chest wall are the consequences of this inequality. The latter can be shown by drawing the outlines of the chest in both respiratory phases as seen in Figure 18*C*. Increase in convexity of the chest wall becomes thus evident. This *balloon-like inflation* can easily be confirmed by simple palpation of the lower hemithorax. Approximate planimetric illustration of this stereometric phenomenon is given by Figure 19, showing the bulge of the chest wall and the enlargement of the costal spaces as a result of various degrees of rib abduction.

The yield of the costal cartilages to the lateral pull of abduction is proved by the

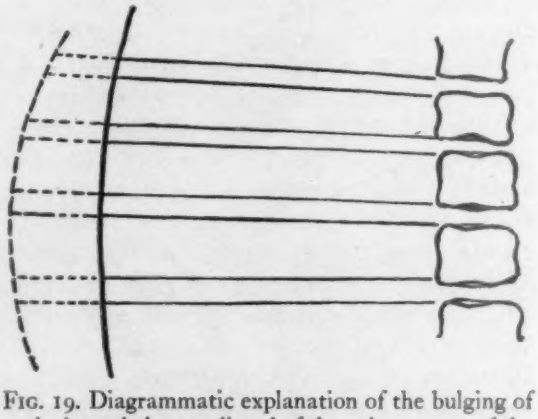

Fig. 19. Diagrammatic explanation of the bulging of the lateral chest wall and of the enlargement of the intercostal spaces caused by the abduction of the ribs in different degrees.

inspiratory widening of the subcostal angle as visible in the newborn. The greater length of these cartilages in the lower hemithorax and the straightening of their angles on inspiration equally promote abduction in the adult. Both phenomena yield further evidence of the fact that the lower hemithorax is specially constructed, in its entirety, in favor of lateral enlargement by means of rotation of the ribs around their vertical axes. *Flank respiration*, brought about in this way and predominant in quadrupeds, may be observed in its proper original form—apart from the breathing motion of the newborn—when examining the rib excursions of man placed "on all fours" or in the prone position. Sidethrust manifests itself in these positions and makes evident that lateral enlargement of the chest may occur without any elevation of the ribs. This is a significant observation disproving the orthodox theory of the "neck axis" of rib excursions.

Further evidence of the pincer-like opening of the lower pairs of ribs has been given by Braune (1889). In the reported case of congenital nonunion of the breastbone he saw inspiratory enlargement of the *inferior* half of the fissure.

When examining roentgenologically the widening of the chest of adults, the disturbing superimposition of rib shadows can be avoided by directing the central ray obliquely from below upward, corresponding to the decline of the ribs. Figure 20 shows the enlargement of the thorax of a healthy adult during *deep* inspiration (abduction plus elevation of the ribs). Drawing the outlines of the ribs upon each other in both phases (Fig. 20*C*) frontal excursions can satisfactorily be analyzed. It is clear that sideward dilatation does not take place but seemingly in the upper hemithorax, where ascension of the pairs of ribs to the level of their narrower upper neighbors is evident, without any or with a minimum of sideward shift. Distinct inspiratory deepening of the thoracic waist is visible at the level of the sixth and seventh segments. Thus this region is relatively "mute" as to the periodic inspiratory as well as to the persistent emphysematous (Fig. 1 and 2) enlargement of the chest cavity. Inspiratory bulging of the thoracic wall (in the sense of the schematic drawing Fig. 19) accounts for the enhanced convexity of the lower hemithorax on inspiration; this is best seen in Figure 20*C* when connecting the lateral contours of the ribs in both phases. Contrary to the usual assumption of a parallel shift of the ribs, it shows balloon-like inflation of the flanks, which can be ascertained by palpation as well.

Deepening or dorsoventral expansion of the rib cage is in its major part no separate movement but a function of elevation. The inclined ribs of the adult approach the horizontal plane when elevated on inspiration, and so their anterior ends shift away from the spine drawing along the sternum.

From a theoretical point of view the backward directed component of deepening (repulsion; *c* in Fig. 17) is of the utmost significance. Repulsion yields the definite proof of the rotation of the ribs on a vertical axis. It has been proved experimentally, in 1881, by the exact measurations of Landerer (quoted in detail by Felix). This author found, in artificial inspiration on cadavers, dorsal displacements of the ribs from the seventh to the eleventh amounting up to 8 mm. In the living there is no difficulty to demonstrate this phenomenon. Palpatory examination of laterally recumbent adults proves the distinct backward inspiratory shift of the lower ribs of the side the subject lies upon. Since abduction is checked in the lateral position by the resistance of the supporting surface, expansion of the rib cage takes place (in the inferior hemithorax) by deepening (and not by "diaphragmatic breathing" as it is generally believed to be).

Repulsion of the costal manubria contradicts sharply the theory which tries to reduce all components of rib excursions to rotation around the neck axis. Backward movement of dorsal rib segments cannot be brought about by the intercostales; it requires *extramural* forces (levatores). As a phenomenon incompatible with both the

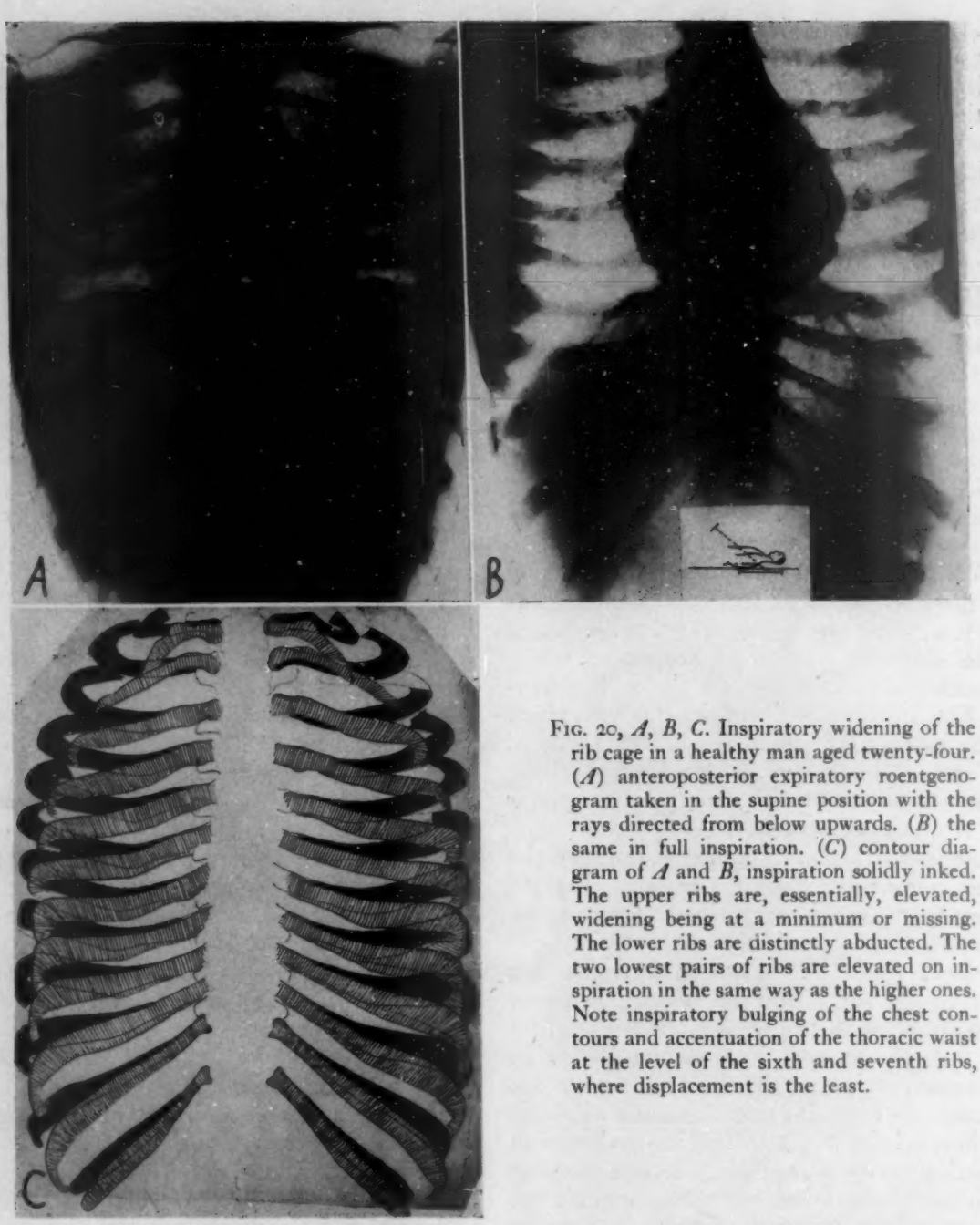

FIG. 20, *A*, *B*, *C*. Inspiratory widening of the rib cage in a healthy man aged twenty-four. (*A*) anteroposterior expiratory roentgenogram taken in the supine position with the rays directed from below upwards. (*B*) the same in full inspiration. (*C*) contour diagram of *A* and *B*, inspiration solidly inked. The upper ribs are, essentially, elevated, widening being at a minimum or missing. The lower ribs are distinctly abducted. The two lowest pairs of ribs are elevated on inspiration in the same way as the higher ones. Note inspiratory bulging of the chest contours and accentuation of the thoracic waist at the level of the sixth and seventh ribs, where displacement is the least.

theories of the neck axis (Bayle and Hamberger) and that of the intercostales (Hamberger, 1727), repulsion has been ignored by most workers. Felix states in his extensive treatise on respiratory mechanics (1928): "Reversal of the forward movement into back-thrust (Rückstoss) has not yet been clarified."* It must be emphasized, however, that repulsion is no indispensable

* As pointed out by Cl. Bernard, J. Thomsen and others, one has always to keep a sharp eye on facts being repugnant to prevailing doctrines. History of science teaches that thorough examination of such a fact is the most frequent cause of new discoveries or new theories by which natural phenomena can be more satisfactorily understood.

prerequisite of abduction. Medial shift of the rib head in its saddle-joint (Fig. 15) allows lateral enlargement in the human thorax just as in that of the gorilla; it results from the biaxial construction of the costovertebral joint. Felix states: "The capitulum can slightly glide forward toward the vertebral body."

Elevation of ribs on inspiration can likewise be examined by double-phased roentgenograms taken in the lateral projection. Figure 21 shows the diagrammatic explanation of such an investigation. It is well seen that the deepening of the upper hemithorax considerably surpasses that of the lower one, elevation being the maximum at the level of the third and fourth ribs and decreasing from here upwards and downwards. This known fact accounts for the inspiratory decrease of the angle of Louis; it disproves at the same time the orthodox scheme of Hamberger which supposes parallel shifts of the ribs rotating around the "neck axis."

Elevation of the eleventh and twelfth ribs takes place in the same way as that of the others (Fig. 20*C*). One-headed tenth and ninth ribs are frequent variations, and it is obvious that all these regressed ribs cannot rotate upon a nonexistent neck axis, but only on a pivot lying in the costovertebral joint and around a horizontal axis directed from back to front. In absence of elevation there is no deepening either, as e.g. in the horizontal ribs of the newborn. Elevation (plus deepening) decreases and widening increases when the course of the oblique ribs approaches the horizontal plane. This occurs, as is known, in the supine position. Braus states (1921): "Sideward excursions of the ribs are smaller in the erect posture than in horizontal recumbency." This readily observable and measurable fact also refutes the neck axis theory which assumes *compulsory* movements of the ribs. This means that the ribs had to follow a course determined by the situation of the unique axis, like a door on its hinges; in this case changes in the course of excursions would be unimaginable. Contrary to this, the theory of biaxial rib movements agrees with all practical experiences.

This new theory receives further confirmation by the study of the prime motive power of the biaxial rib movement consist-

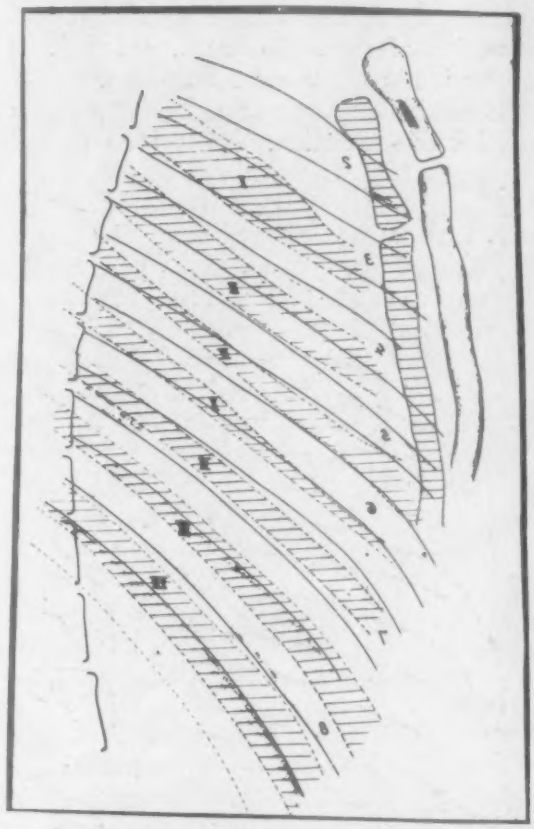

Fig. 21. Diagram showing inspiratory deepening of the rib cage in a healthy man (same as in Fig. 20.) Deepening is much more marked in the superior hemithorax. The angle of Louis decreases on inspiration.

ing in the levator system. In the human the arrangement of these muscles is such that their thickness and length increases gradually from above downward. Resolving the pulling force of the oblique muscle by the parallelogram of forces (Fig. 22) the vertical *elevating* and the horizontal *abducting* components can be distinguished. The length of the costal manubria, which afford attachments to the levatores, increases cephalocaudally (Fig. 3 and 22). This is due partly to the progressive sideward shift of the costal angles, partly to the shortening

and backward declination of the transverse processes. It is clear that the horizontal power arm elongates absolutely as well as relatively when proceeding downwards. This segmental increase of the abducting component is in harmony with the above mentioned structural differences in the construction of the osteothorax, which favor abduction in the lower hemithorax.

Elevation of the first pair of ribs requires special consideration, for it is governed otherwise than that of the lower ribs. The first costovertebral joint differs considerably from those from the second to the tenth: (a) the head of the first rib joins only one vertebral body; (b) it is spherical in shape and *the dividing crest of the surface is missing;* (c) the articular cavity is likewise spherical and greater and deeper than that of the other costovertebral joints (Fig. 23). Instead of a saddle-joint we find thus a typical ball-and-socket joint. I found this peculiar attachment present also in the skeleton of the great anthropoid apes (chimpanzee and gorilla; see Fig. 24). This apparatus aims at the fulfilment of particular mechanical requirements.

Elevation of the upper thoracic inlet is produced by an intrinsic force of its own, viz. the scalenus group, which supplies the most effective accessory force of inspiration. The scaleni are inserted on both topmost ribs far from the fulcrum and act

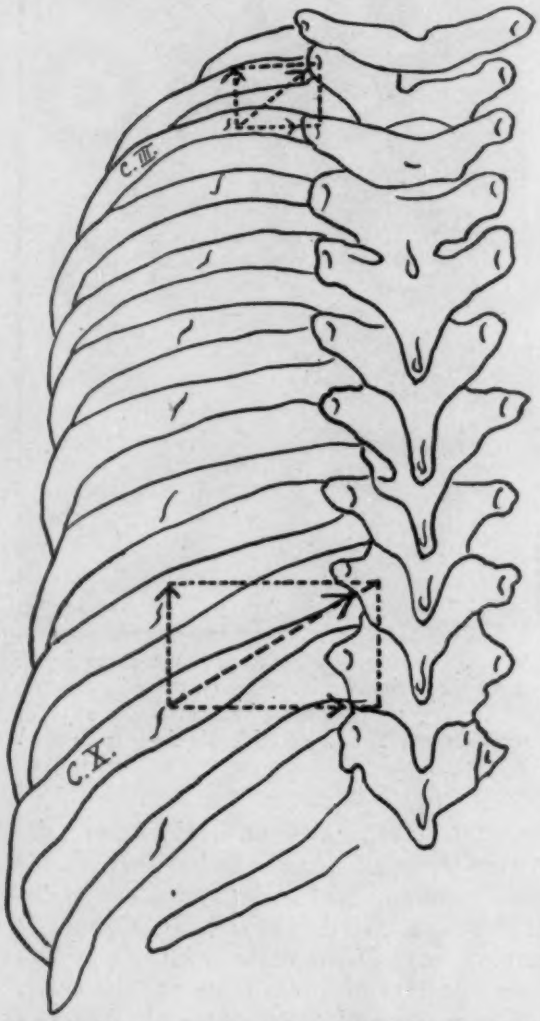

Fig. 22. Diagrammatic explanation of the segmental changes of the human levator system. Absolute and relative increase of the horizontal-abducting force-component of the levator in the lower hemithorax.

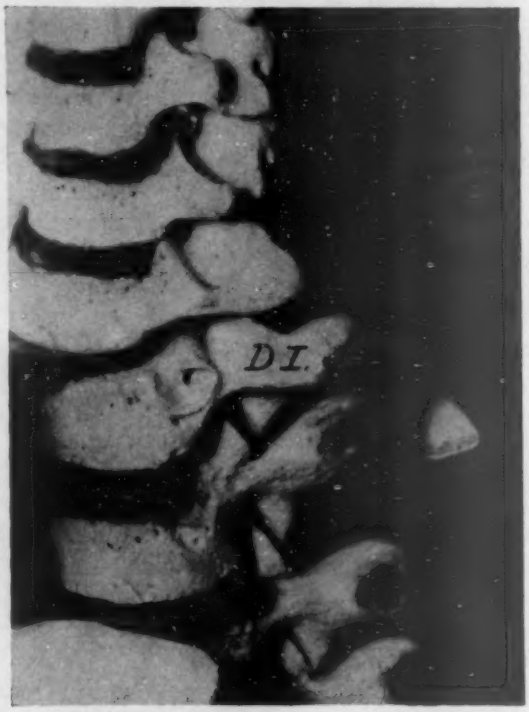

Fig. 23. The articular facet of the first thoracic vertebral body is a regular spherical section in man.

therefore on a very long power arm, i.e. with the best leverage. Elevation by the scaleni rotate the first pair of ribs around a horizontal axis which runs *transversely* (Fig. 25), contrary to the sternovertebral elevatory axis of the levatores. This axis coincides fairly well with the course of the rib neck, and it is conceivable, therefore, that this coincidence induced several workers to regard the "neck axis" as the general governing principle of the movements of *all* ribs.

The action of the scaleni enlarges the chest cavity upward and particularly forward by extensive propulsion. Their contraction can readily be observed by palpation and found as a rule in "upper thoracic breathing" (or "heaved breast"), in yawning, emphysema, asthmatic attack and other cases of labored breathing.

FIG. 24. First, second and third thoracic vertebrae of a gorilla showing the relative size and concavity of the costovertebral facet D1.*

* Figures 13, 14, 15, 16 and 24 were taken from specimens of the Musée Zoologique, Genève. Courtesy of Professor P. Reveillot.

CONCLUSIONS

The above studies indicate that the basic biaxial rib movement, consisting of abduction around a vertical and elevation around a horizontal axis, as present in primitive reptiles, determines similar respiratory rib excursions also in man. The different bony structure of the upper and lower hemithorax accounts, however, for different manifestations of these two basic movements in the respective parts of the chest. Abduction is checked in the *superior* hemithorax owing to the mechanics of the upper limbs, which require strongly attached two-headed ribs. Elevation, on the other hand, is favored there and promoted by the suitable arrangement of bony and muscular components. The formation of the *inferior* hemithorax furthers largely abduction when making possible horizontal enlargement by means of repulsion of the costal manubria. This latter kind of movement takes advantage from the gradual caudal shortening of the transverse processes, of the change of the costotransverse articulations into arth-

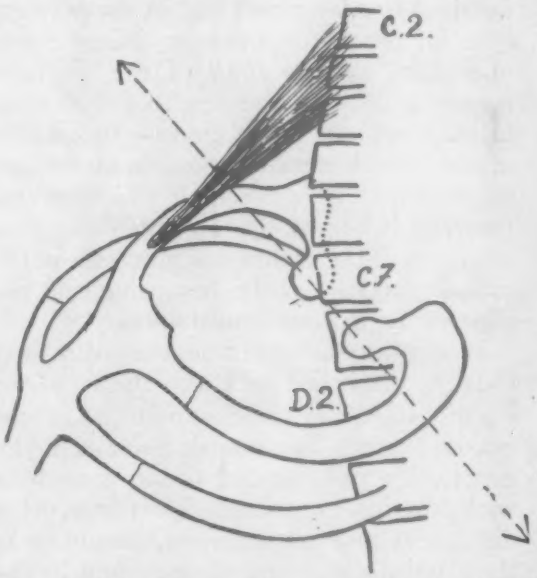

FIG. 25. Diagram to illustrate the action of the scaleni which rotate and elevate the superior thoracic opening on a transverse-horizontal axis.

rodia, as well as of the regression of the ribs towards one-headedness.

The functional rôle played by the costotransverse joints is an essential part in this mechanism. Free saddle-joints of the rib heads would allow excursions (i.e. circumduction) to a large extent. Yet the *breaking effect* of the costotransverse joints determines the *extreme limit* of the displacements; it compels the ribs to follow some principal courses out of the various kinds of motion which were practicable in a single saddle-joint. This checking and directing function is helped by the buffer-like construction of the transverse processes in the superior and by their shortening and decline in the inferior hemithorax.

It may be concluded from the above facts that the disproved neck axis theory of the rib movements is to be substituted by the biaxial theory. This new doctrine is phylogenetically well founded and in agreement with practical experience. Apart from other difficulties and inadequacies, absurdity of the classical theory becomes evident by the following reflection. If the ribs were rotated around the neck axis, the fixed point of the movement would be removed to the breastbone in the prone position; consequently every inspiration ought to entail a caudal shift of the whole spine. This apparently does not occur; in place of that lateral enlargement, i.e. widening by increased abduction, compensates for the lack of elevation.

From a didactic point of view the dilatation of the chest cage may be demonstrated as follows. Place the hand on the table with the ulnar border facing downwards as if clasping a tumbler, spread the curved fingers then as if you would enclose a larger diameter. The fingers thus stretched in different degrees move away from one another (in their saddle-joints) in a fan-like manner and imitate fairly well the inspiratory movement of dorso-axillary rib portions.

From all our inquiries we may infer that the controversial and repeatedly criticized old theory which regards the intercostales as the real movers of the ribs is to be revised. This theory follows from the assumption of a neck axis and explains lateral expansion of the chest as a secondary phenomenon resulting from the elevation of the ribs. Contrary to this, isolated widening of the rib-cage is a readily observable phenomenon in the newborn and in adults when in the horizontal position. Other inadequacies of the intercostales theory have been exposed by several workers and by the writer in a previous paper as well. On the other hand, the new doctrine is founded on the comparative morphology of the skeleton and agrees with all observations including those being unexplainable by the neck axis theory. The principal conclusion of the above studies is, therefore, *to regard the muscle system of the levatores costarum as the most effective and most essential prime motive force of inspiration.*

SUMMARY

1. The thoracic cage must be divided into an upper and a lower hemithorax with due regard to the junctions and the movements of the ribs. This bipartition is externally marked by the lateral thoracic furrow.

2. The mechanical basis of rib excursions is their rotation around two axes, one vertical, the other horizontal; addition of both results in the circumduction of the ribs. This biaxial principle is phylogenetically well founded; it is the governing rule of the rib movements in lower vertebrates as well as in mammals.

3. Differences in the bony and muscular construction of the upper and lower hemithorax account for the different manifestations of both basic movements. Rotation on the vertical axis provides for lateral enlargement by abduction of the ribs and is favored by the bony structure of the inferior hemithorax. Elevation, on the other hand, takes place by rotation on the horizontal axis and is assisted by the special arrangement of the mechanical components of the superior hemithorax.

4. The disproved neck axis theory entails the assumption that the intercostales

are the movers of the ribs. As opposed to this, the biaxial principle of rib movements leads automatically to the conclusion that the principal moving force of inspiration is provided by the muscle system of the levatores costarum.

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SMALL INTESTINAL PATTERN IN SPRUE AND SIMILAR DEFICIENCY DISEASES

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IN THE past, roentgenological examination of the small intestine has been more or less neglected. One reason for this has been the failure to recognize that small intestinal lesions could frequently be discovered and treated. It was not until 1932 that Crohn, Ginzburg and Oppenheimer[1] called attention to a new disease entity, regional ileitis, and it was only in 1934 that Snell and Camp[2] demonstrated small intestinal changes in deficiency states, such as sprue. A second reason for neglecting the study of the small intestine is inherent in the method. A great deal of time and effort is necessary for a roentgenological study of the small intestine; therefore, this type of examination is frequently limited to those cases in which a lesion of this part of the intestinal tract is suspected on the basis of clinical data.

FIG. 1. Normal small intestinal pattern forty-five minutes after drinking barium solution followed by ice water.

The accepted standard of roentgenological study of the small intestine consists of frequent roentgenographic and roentgenoscopic observations following an examination of stomach and duodenum. This method permits the study of a few loops of small intestine at a time. In 1939 Gershon-Cohen and Shay[3] proposed a different method of studying the anatomical outline of the small intestine. They introduced a duodenal drainage tube and poured a barium-water solution directly into the duodenum. In 1943 Schatzki[4] used the same method independently, calling it "small intestinal enema." With this technique he was able to fill the entire small intestine from pyloric sphincter to cecum within approximately twenty minutes. The method is most valuable when one is concerned with the problem of finding a localized small intestinal lesion. Generalized changes of the small intestine are better studied by an oral water-barium meal.

We give an initial 8 ounces of a barium-water solution (barium and water in equal proportions) followed by a small amount of ice water. The ice water enhances small intestinal peristalsis,[5] so that frequently the entire small intestinal pattern can be studied within one hour and a half after the barium intake in the normal individual. In this way one can outline the majority of small intestinal coils simultaneously on survey roentgenograms. A roentgenoscopic observation is made about thirty to forty minutes after the start of the examination, and again when the barium has filled the lower ileal loops. Usually a supine film is

taken at forty minutes (Fig. 1) and a prone film in one and a half to two hours (Fig. 2) after the start of the examination. By this simple procedure a fairly complete demonstration of the small intestine may be obtained and a number of unexpected lesions diagnosed.

The length of the living small intestine[6,7] depends upon the tonus of the longitudinal muscle. It varies in different individuals and probably varies from time to time in the same person. Patients of a pyknic habitus usually show a hypertonic type of small intestine. Patients of an asthenic type usually show wider small intestinal loops. In the healthy individual a continuous stream of barium outlines the coils of the small intestine. The jejunum shows the so-called "herringbone" pattern. The circular folds decrease in size from above downward.

It is stated that the early stage of sprue[2,8,9,10] is characterized by hypermotility and hypertonicity; late stages show hypomotility and hypotonicity. The passage of barium through the small intestine is markedly delayed and the intestinal loops are dilated. There is abnormal segmentation, coarsening of folds, moulage sign and, in some cases, a sedimentation effect of the barium, such as is seen in the stomach in cases of gastritis.

The question arises whether this pattern of the small intestine is always present in cases of sprue and whether it has differential diagnostic significance. Before this is discussed, it should be stated that the term "sprue" applied in this paper includes the tropical and nontropical varieties as well as celiac disease. These three diseases are probably but different stages of one disease entity.[11] The identity of these diseases has been suggested by studies showing that the anatomical changes in these three diseases, as well as their clinical course and response to therapy, are fundamentally the same. One generally considers the tropical variety to be the earlier form of the disease.

In a paper published by Snell[11] it was shown that out of 6 cases of tropical sprue only 1 had roentgenological changes of the small intestine, while out of 32 of the nontropical variety, 20 showed small intestinal changes. Since then, Suarez[12] and Menendez[13] have studied large series of cases of tropical sprue and found changes to be demonstrable in the small intestine in 75 per cent.

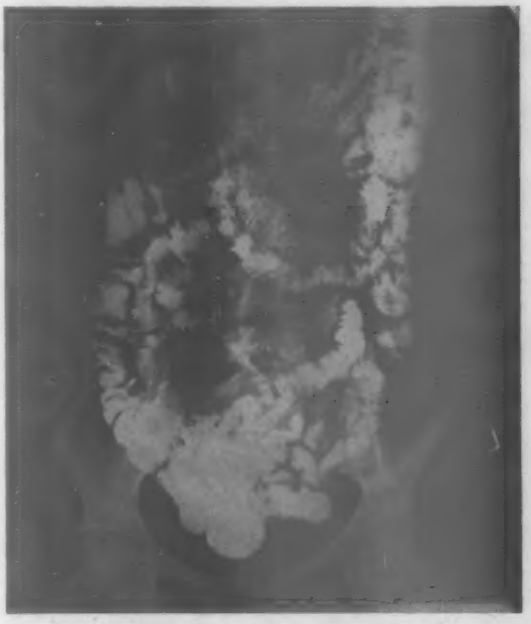

Fig. 2. Normal small intestine one and a half hours after beginning of examination. A fairly complete outline of small intestinal loops is obtained.

The high incidence of small intestinal changes in this disease brings up the question of whether these changes could possibly be considered to represent the primary disorder. A final answer to this question is not yet available.

Snell[11] summarized the sequence of events in sprue in the following manner: "A lack of some unknown factor in diet, probably to be identified with some portion of the vitamin B complex, or a failure of the intrinsic factor in gastric juice may lead to failure of formation of certain products of digestion essential to the proper activities of the blood-forming organs and of the gastro-intestinal tract. This deficiency, if not corrected, leads to progressive failure

of the absorptive function of the small intestine." At any rate, early in the disease, the small intestinal function is seriously disturbed and, once this function is altered, a variety of secondary nutritional deficiencies occurs. The main clinical symptoms of sprue are: (1) digestive disturbances, bloating and abdominal pain, and diarrhea; (2) anemia of the hypochromic or hyperchromic type; (3) various nutritional deficiencies: (a) defective fat absorption producing fatty stools, (b) defective carbohydrate absorption recognized by a flat oral blood sugar curve, and (c) defective protein absorption indicated by hypoproteinemia (peripheral edema). Various vitamin deficiencies also occur. Vitamin A deficiency has been reported, although only rarely. Vitamin B deficiency is frequent, producing pellagra-like symptoms and pigmentation. Vitamin D deficiency is responsible for the low calcium values in the blood with associated osteoporosis of the skeleton, and vitamin K deficiency is indicated by hemorrhagic tendencies of some sprue patients. Two of our patients died from intestinal hemorrhage. As a result of the poor absorptive function of the small intestine, patients with advanced sprue are markedly emaciated and give the history of enormous weight loss. Once the picture is developed to its full extent, intestinal impermeability represents an irreparable stage of the disease and this usually interferes with effective substitutional therapy. Effective therapy can be expected only if the diagnosis is made early enough to prevent a vicious circle from occurring. In our small series of 12 cases of deficiency diseases, the roentgenological findings gave the clue to the proper diagnosis in 2 instances, and possibly in a third. In these 3 cases, the classical clinical symptoms of sprue were lacking. There was abdominal distention and peripheral edema, but there was no evidence of fatty stools and the oral glucose tolerance curve was normal. The diagnosis of a nutritional disturbance was not established prior to roentgenological studies.

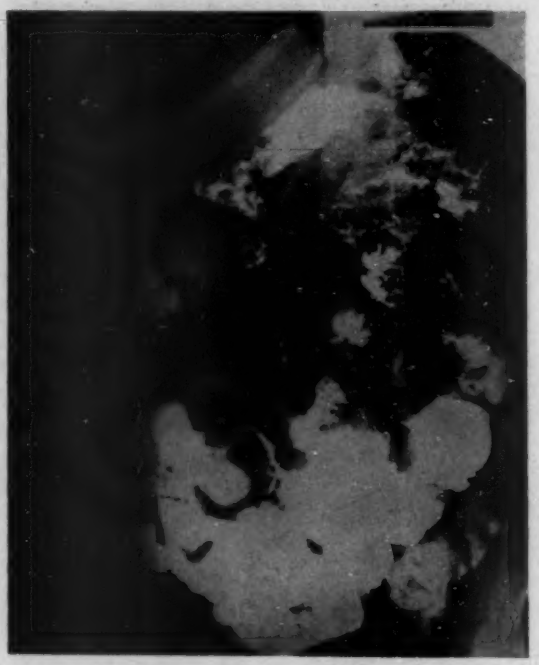

FIG. 3. Case 1. (June, 1943) Grossly abnormal small intestinal pattern; markedly distended loops alternating with markedly contracted loops; greatest degree of distention in mid-jejunum. Delayed passage time.

REPORT OF CASES

CASE 1. B. G., female, housewife, aged thirty-one, was admitted to the hospital on June 11, 1943, and discharged on June 15, 1943. The chief complaints were edema of the feet and ankles, excessive fatigue and pain in the left flank. The past history was not remarkable, except for bilateral resection of the ovaries for small cysts in 1936. There was a gradual weight loss of 8 to 10 pounds and a tendency towards diarrhea for six to seven years. The physical examination was not remarkable, except for a distended abdomen and some peripheral edema. The laboratory findings showed a moderate hypochromic anemia. Serum protein was 4 mg. (normal 6.5 to 7.5 mg.), the albumin fraction 2.14 mg. (normal 4 to 5 mg.), and the globulin fraction 1.86 mg. (normal 2 to 3 mg.). The small intestinal changes present in this patient indicated severe nutritional disturbance, possibly nontropical sprue (see Fig. 3). The time of pas-

sage of the barium through the small intestine was markedly prolonged. The patient was put on a high protein, low fat diet and also received various vitamins and crude liver extract by injection. She was readmitted a year later, in August, 1944. At that time she still had a tendency towards diarrhea, but she felt better in general and had gained weight and was less fatigued. The abdomen was still distended, and there was still edema of the ankles and legs. The patient, however, had not regularly received the liver extract. At this time additional laboratory studies were carried out. There were no fatty stools on a Schmidt diet.* The oral glucose tolerance curve was low, but still within normal limits. The roentgenological aspect of the small intestine had not changed (Fig. 4). Due to the current interest in the reaction of the small intestine to various drugs, we observed the effect

FIG. 4. Case 1 (August, 1944) after parenteral liver and dietary therapy; no change of pattern demonstrable.

of prostigmine in this patient. We gave 0.75 mg. subcutaneously. Prompt and striking contraction of many loops occurred (Fig. 5). The patient was seen again on February 25, 1946. In the meantime, she had continued on an antisprue management, but had added bananas to

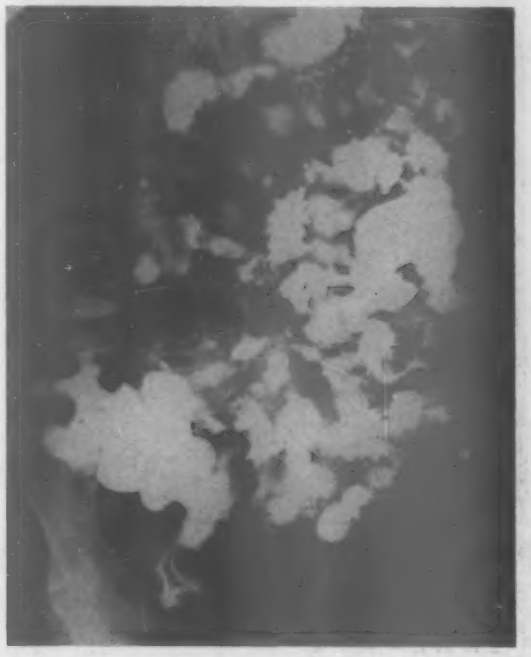

FIG. 5. Case 1. (August, 1944). Forty-five minutes after subcutaneous injection of 0.75 mg. prostigmine, considerable contraction of the distended loops takes place.

her diet which, according to her, best controlled the diarrhea. Re-examination still showed an abnormal pattern, but the contracted loops outnumbered the dilated ones (Fig. 6). Again prostigmine was given and an effect similar to the previous one observed (Fig. 7). After this examination the patient was put on folic acid and a regular diet. This alone did not adequately control the patient's symptoms, and it was necessary to modify the treatment. While the general state of health of the patient improved under the different regimens, the abdominal distention and the edema persisted in varying degree.

To summarize, a patient with abdominal bloating, diarrhea and ankle edema showed generalized abnormal pattern of the small intestine indicative of nutritional disturbance. The abnormal pattern was gradually modified in the course of three years, during

* Schmidt diet as modified by Pratt consists of 102 gm. protein, 132 gm. fat, 180 gm. carbohydrate daily for three days. (Pratt, J. H. A study of steatorrhea, with special reference to its occurrence in pancreatic disease and sprue. *Am. J. M. Sc.*, 1934, *187*, 222–235.

Fig. 6. Case 1 (February, 1946) after further therapy. Film taken one hour and twenty minutes after barium. Deficiency pattern still obvious, but there is now an increased number of contracted loops; mid-jejunal loops still distended. Marked improvement of passage time.

Fig. 7. Case 1. (February, 1946) Injection of 0.75 mg. prostigmine increases motility and produces contraction of loops.

which the patient received various forms of antisprue therapy. There was a definite return toward normal on liver extract and dietary management along with clinical improvement.

Case 11. R. B., female, housewife, aged twenty-six, was admitted to the hospital on

Fig. 8. Case 11. (May, 1944). One hour after intake of barium, small intestine fantastically distended. Small intestinal passage of barium lasted more than seven hours.

May 18, 1944, and discharged on May 29, 1944. The chief complaint was bloating and gas pain, crampy in character, increasing with distention and nausea. The illness which caused admittance had started a year previously. The legs became swollen and menstruation ceased. There was a tendency towards constipation. The patient had lost about 9 pounds in weight. She had had the same symptoms six years previously for the duration of one year. The physical findings

were not remarkable, except for a distended abdomen and pitting edema to mid-thighs on both sides. The clinical diagnosis was that of ileus. The roentgenological study showed an abnormal pattern characteristic of a generalized disturbance, interfering with proper absorptive function (Fig. 8). One could not be certain whether the abnormal pattern was of an inflammatory nature or represented a deficiency state. On the Schmidt diet the patient had no evidence of fatty stools. The oral blood sugar curve was normal. Serum protein was low, and there was a moderate secondary anemia. The patient was discharged on a high caloric diet and crude liver injections were recommended. When she was re-admitted in July, 1945, about a year later, the swelling of legs and ankles had improved but flatulence was still present. She was no longer constipated, but had regular, well formed movements. Menstruation had recurred. Serum protein was 4.33 mg. (normal 6.5 to 7.5 mg.), albumin 3.6 mg. (normal 4 to 5 mg.) and globulin 0.73 mg. (normal 2 to 3 mg.). Cephalin flocculation test was negative. There was no change in the appearance of the small intestine as compared with the earlier examination. Observations were made with 10 mg. mecholyl (Fig. 9 and 10). There was very active peristalsis three to five minutes after the injection. Some of the narrow segments dilated considerably when a peristaltic wave forced barium through the contracted areas. No observations with prostigmine were carried out. During one of her many hospital admissions, in October, 1944, a peritoneoscopy was performed. There was no evidence of any inflammatory lesions of the small intestine; enormous atony of the small intestine could be seen.

To summarize, a patient without flat sugar curve and without impairment of fat absorption as indicated by the normal result of the Schmidt diet had definite clinical evidence of disturbance of protein metabolism (peripheral edema) associated with small intestinal changes.

Case III. The patient, a female, aged sixty-seven, was admitted to the hospital on August 31, 1938, and discharged on September 17, 1938, for diplopia, painful joints and weight loss. She had poor dietary habits, anorexia but no abdominal pain and slight constipation. Physical examination showed limitation of

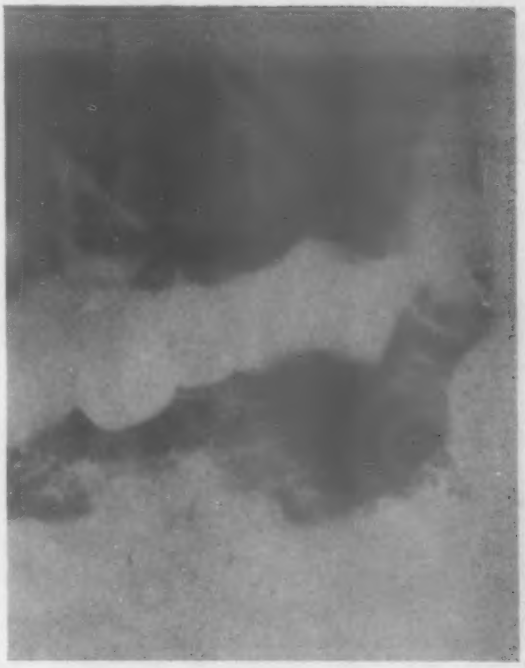

Fig. 9. Case II. (July, 1945). No change of small bowel pattern after dietary and liver therapy. Patient clinically improved. Close-up of one mid-jejunal loop.

Fig. 10. Case II. Same loop three minutes after 10 mg. of mecholyl. Marked contraction observed.

FIG. 11. Case III. (1938) Examination showed cardiospasm and normal small intestinal pattern.

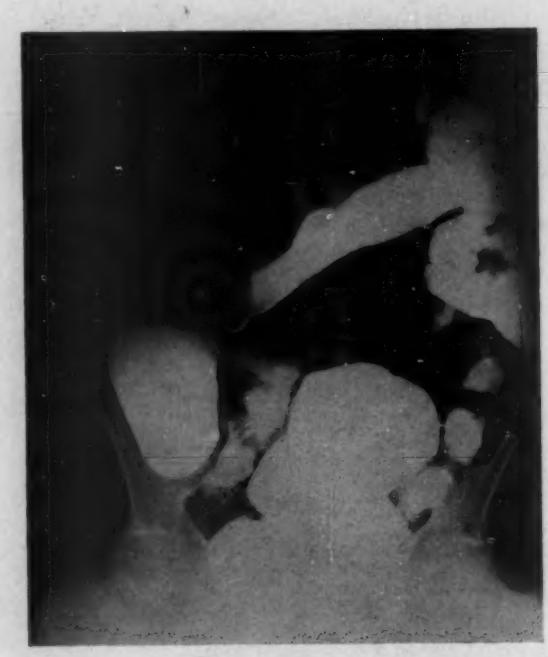

FIG. 12. Case III. (October, 1942) Barium enema. Colon simulates scarred stage of ulcerative colitis. Note smooth contours but no marked shortening of colon.

joint movements and sixth nerve paralysis. Cardiospasm was observed by roentgen examination. The small intestinal pattern was normal (Fig. 11). She had hypochromic anemia. A high vitamin, high caloric diet and iron medication were advised. The patient was discharged and returned four years later when she was admitted for nausea and diarrhea, abdominal pain and weight loss. She had a distended abdomen, pitting edema of both legs and skin changes of the pellagra type. There were severe roentgenological changes of the colon similar to

FIG. 13. Case III. (November, 1942) Marked distention of entire small intestine.

the changes seen in ulcerative colitis after marked scarring develops (Fig. 12), and she had dilatation of the small intestine, consistent with a severe nutritional disturbance (Fig. 13). A plain roentgenogram (Fig. 14) showed a step-ladder appearance of the small intestine, as in ileus. It has been reported[14] that patients with this disorder have been operated upon because their symptoms have been mistaken for ileus. If one considers the roentgenogram (Fig. 14) one certainly has to admit that without clinical data the diagnosis of an acute abdominal emergency (ileus) would have to be made. Roentgen diagnosis was not definite inasmuch as two possibilities were considered: (1) ulcerative co-

litis with secondary small intestinal changes, such as reported by Mackie and Pound;[18] (2) deficiency state with involvement of both small and large intestines. The patient was discharged after having had two esophageal dilatations for persistent cardiospasm. She was advised to take vitamins and crude liver extract. When seen twice again, after this admission, she had not responded to therapy and her course was rapidly retrogressive. The small intestinal pattern became progressively worse, changing from widening and coarsening of folds to moulage sign and severe segmentation (Fig. 15). She died on October 21, 1943. Autopsy findings showed extreme atony and dilatation of the entire small intestine, chronic pigmented duodenitis and jejunitis, atrophy of mucosa and lymphoid tissue of ileum, chronic or healed colitis, intermittent scarring and dilatation of the entire colon and sigmoid. Histopathologically, atrophy and edema of all coats of the intestines were found.

FIG. 14. Case III. (November, 1942) Plain film of abdomen; greatly distended small intestinal loops simulating ileus.

FIG. 15. Case III. (June, 1943) Marked moulage sign. Notice progression of deficiency pattern in agreement with clinical retrogressive course.

ROENTGENOLOGICAL CHANGES IN DEFICIENCY STATES

As can be seen from the few case illustrations, there is considerable variation in the roentgenological appearance of the small intestine of patients with deficiency syndromes. Most frequently, changes are limited to the jejunal and upper ileal loops. The lower ileal loops are not involved, while abnormalities are occasionally observed in the duodenum[2] (Fig. 16). In some patients delayed motility with dilatation of loops was prevalent; in others, effacing of the normal pattern (moulage sign); and in still others, alternation of dilated and contracted loops. It is also worth mentioning that the abnormal pattern may only become obvious late in the examination (Fig. 17 and 18).

It was, however, not possible to correlate specific patterns with specific absorptive deficiencies, nor was it possible to correlate the degree of roentgenological disturbance with the patient's clinical state of health.

As reported above, a few observations on the effect of drugs, such as prostigmine and mecholyl, upon the appearance of the small intestine of patients with sprue have been made. The patients were observed roentgenoscopically and an impression of

Fig. 16. A. R., young male. Five years of diarrhea. abdominal cramps. Note that abnormal pattern begins in the duodenum.

Fig. 17. C. B., male, aged fifteen. Film taken about thirty minutes after beginning of examination. No gross abnormality noted.

the intestinal motility was obtained and a roentgenogram taken. Further roentgenoscopic observations were made following the administration of the drug, and the roentgenoscopic observations were recorded on spot films. Two cases in this group showed a normal response to prostigmine (Fig. 4, 5, 19, 20). This observation is in contrast with those made by Ingelfinger and Moss.[14]

Fig. 18. Same case. Three and a half hours later. Marked segmentation of small intestinal pattern is apparent.

Following effective sprue therapy, there was a return of the roentgenological appearance towards normal in some patients, while in others the improvement of the clinical status on an efficient antisprue management was not accompanied by a corresponding improvement of intestinal pattern. Miller and Rhoads[16] reported complete return of the abnormal pattern to normal, while Golden[9] reported improvement, but not complete return to a normal pattern in fairly advanced cases of sprue. Recently Spies[17,18] reported very striking

Fig. 19. D. H., male. Clinical diagnosis of sprue. Film two hours after intake of barium. Dilated loops of small intestine.

Fig. 20. Same case. Forty-five minutes after injection of 0.75 mg. prostigmine. Contracted loops have become apparent; also, segmentation and moulage sign.

restoration of small intestinal pattern following folic acid therapy. In a number of cases of celiac disease, not included in this report, we had the same experience. Drew, Dixon and Samuel[19] found serial roentgenological observations in sprue patients valuable for the assessment of clinical improvement.

DISCUSSION OF CLINICAL DATA

As far as the clinical data are concerned, we would like to limit ourselves to just two statements:

(1) In tabulating the results of blood sugar tolerance curves, values of serum proteins and fat contents of stools in 12 cases, it became apparent that patients with small intestinal disturbance may exhibit deficiency of absorption of any one or more of the major food constituents. In other words, there was no correspondence in the disturbance of absorption of fat, carbohydrate and protein in a given case. This is not too surprising, if one considers that each one of these materials is absorbed by a different and highly complicated mechanism.

(2) The frequency of the association of abdominal distention and peripheral edema has been rather striking. An analysis of 32 cases of nontropical sprue from the Mayo Clinic[11] showed that peripheral edema was present in 14 cases and absent in 18 cases. In our series, it was present in 8 and absent in 4 cases. Since all of the cases had abdominal symptoms and most of them showed edema, the combination of these two signs seems to occur with sufficient frequency to make it a valuable diagnostic complex.

ROENTGENOLOGICAL DIFFERENTIAL DIAGNOSIS

We have yet to discuss the problem of whether or not the roentgenological small

intestinal changes are always indicative of primary nutritional disturbances. We can state immediately that the same changes may be observed in patients who are suffering from so-called "secondary sprue."[20] This is a fully developed sprue syndrome on the basis of interference of the lymphatic flow from the intestine by disease of the mesenteric lymph nodes. The same roentgenological small intestinal findings may be present in these patients and the diagnosis can be suspected clinically only if peripheral lymph nodes complicate an otherwise fairly typical picture of sprue.

The main differential diagnostic consideration in patients with abnormal small intestinal pattern is: generalized granulomatous jejuno-ileitis, an inflammatory disease of the small intestine, apparently related to regional ileitis. The initial stages of this inflammatory disease cannot always be differentiated roentgenologically from sprue. An inflammatory disease of the small intestine may start with what seems to be a deficiency pattern. Sussman and Wachtel[21] published cases which started with a deficiency pattern and later changed to a typical granulomatous jejuno-ileitis. They point out that the frequency of involvement of the lower ileum in jejuno-ileitis is a helpful differential diagnostic sign. As a rule the ileum is not involved in deficiency diseases.

DISCUSSION OF VARIOUS THEORIES CONCERNING THE SPRUE PATTERN

Most of our knowledge of the anatomical changes in sprue is based almost exclusively on severely advanced cases which came to autopsy.[9] Atrophy of the mucosa and all the intestinal coats as well as submucosal edema has been reported. Explanations of the less advanced stages of the abnormal small intestinal pattern in sprue have no anatomical basis, since surgical intervention is not indicated in these patients and autopsy material is practically unavailable. Various theories have been advanced to explain the roentgenological pattern. Some authors believe that the fatty content of the intestine in patients with sprue may be responsible for the appearance of the small intestine in the roentgen examination. Studies of the physiology of the small intestine carried out by Pendergrass[22] and his coworkers, who were interested in small intestinal motility under various physiological conditions, are usually quoted as proof of this theory. They studied, among other conditions, the small intestinal pattern after addition of olive oil to the barium meal. The resulting pattern very much resembled that of sprue. Dilatation of jejunal loops, delayed passage and coarsening of folds were apparent. A smudged appearance of the barium and segmental distribution also showed on the roentgenogram. There can be, therefore, no doubt that fatty contents may produce a "deficiency" pattern. Under the conditions of roentgenological studies, however, the small intestine is empty. Furthermore, the deficiency pattern is present in patients without fatty stools.

A second theory which has found many supporters and which seems to have a good many arguments in its favor is the hypothesis that hypoproteinemia associated with intestinal edema may be responsible for the pattern. Barden[23] and others have shown that dogs, in whom hypoproteinemia with associated edema of the intestinal wall was produced experimentally, showed marked changes of intestinal motility and patterns resembling sprue. Jones and Eaton[24] demonstrated that patients in whom hypoproteinemia occurred postoperatively, because of massive intravenous fluids, also showed edema of the intestines and disturbance of intestinal motility. Diseases not related to sprue but associated with hypoproteinemia, such as nephrosis and liver cirrhosis, frequently show a deficiency pattern. This theory leaves unexplained those cases which do not have hypoproteinemia but show a deficiency pattern. One must conclude, therefore, that hypoproteinemia probably plays an

important role but cannot be the sole factor in the production of the abnormal pattern of the small intestine. Golden[9] believes that the fundamental disorder in these cases is the damage of the intramural ganglion cells. Among other evidence, he reports on histopathological findings obtained in a case of sprue at the occasion of a biopsy in which definite vacuolization of the intramural ganglion cells of the small intestine was seen microscopically. This theory would best explain the fact that the sprue pattern occurs under so many different conditions. The theory that the intramural nerve system is at fault seems to have found support in some experiments of Ingelfinger and Moss.[14] They showed that prostigmine, the anticholinesterase, is ineffective in sprue, while mecholyl produces normal stimulation in sprue patients. They concluded that patients with sprue are lacking in production of acetylcholine and that, therefore, prostigmine, the accelerating effect of which is normally produced by an inhibitory effect upon the acetylcholine destroying cholinesterase, remains ineffective. Hodges, Rundles and Hanelin[25] have recently reported some interesting observations on patients with a variety of disturbances of the intrinsic and extrinsic nerve supply of the small intestine. Further investigations of the influence of drugs upon the motility of the small intestine may help to clarify the mechanism of functional abnormalities of the small intestine in sprue.

CONCLUSIONS

The foregoing observations show that roentgenological studies of the small intestine may help to establish conclusively the diagnosis of a deficiency state in cases in which a clinical diagnosis is difficult; such studies might also contribute towards a better understanding of various nutritional disturbances other than sprue.

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DOUBLE GALLBLADDER

ROENTGENOGRAPHIC DEMONSTRATION OF A CASE OF THE "Y" TYPE; CLASSIFICATION OF ACCESSORY GALLBLADDER*

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DOUBLE gallbladder is a rare anomaly. Wilson[17] found 36 examples reported up to January, 1936, as referred to in articles by Boyden[3] (1926—20 cases), Slaughter and Trout[13] (1933—12 cases), Weiss[16] (1935—3 cases) and Gross[8] (1936—1 case). Additional instances were noted by Wilson[17] (1939), Bryan[4] (1940), Millbourn[11] (1940—2 cases), Alfredo[1] (1940), Stolkind[14] (1940), Walters and Snell[15] (1940—4 cases), Scott, Sanes and Smith[12] (1941), Golob and Kantor[7] (1942—2 cases). No specific reference is made in the *Quarterly Cumulative Index Medicus* for 1943, 1944, and 1945 to reports of cases of double gallbladder. In 1946 one case was reported by Haight,[10] another by Guyton.[9] Together with the present case, therefore, a total of approximately 52 cases had been recorded to the end of 1946. Doubtless other reports of this anomaly have been overlooked.

It should be noted that the term "double gallbladder" as used in many of the above-cited articles is loosely applied to both the divisa (divided) gallbladder and the true duplex (double) type. Hence, true double gallbladder (with two cystic ducts) is even less common than suggested above, and the "Y" subtype (two cystic ducts uniting to form a common cystic duct) rarer still. The exact incidence of the various types cannot be given with accuracy. Using the term "accessory gallbladder" to include both the duplex and divisa varieties, Boyden noted only 5 cases in " . . . over 19,000 reports of cadavers and patients" (about 1 in 4,000) and epitomized an additional 15 culled from the literature. Of these 20 cases, 17 were double gallbladder but only 8 could be further subclassified into the "Y" type (4 cases), and the ductular type (4 cases).

Climan[5] (1929) was probably the first to demonstrate double gallbladder by cholecystography. Bryan[4] (1940) found less than 40 cases reported in the literature and only 8 cases shown roentgenographically. In his case, the ninth, the termination of the two cystic ducts was not determined. Golob and Kantor[7] (1941) indicated that their 2 cases represented the seventh and eighth instances of double gallbladder disclosed by roentgen ray. The cystic ducts were not shown and the patients were not operated upon. Scott, Sanes and Smith[12] (1941) stated that 9 cases have been detected roentgenographically, theirs, the tenth, being verified by operation. In Haight's report[10] (1946) there was roentgen demonstration of a double gallbladder and one cystic duct. Another cystic duct was presumed to be present. The rarity of double gallbladder in roentgenological practice is further attested to by Bell[2] who had never seen one in an experience which included over 20,000 gallbladder examinations at the Long Island College Hospital. The present report is apparently the first recorded instance of a clear roentgen visualization of two gallbladders and two cystic ducts uniting to form a common cystic duct, thus permitting accurate subclassification into the "Y" type.

Various classifications of aberrant biliary vesicles have been made (e.g. Boyden, Weiss). Boyden's anatomical and embryological studies, which included several species of domestic mammal as well as man, are most exhaustive and scholarly, and his interpretations of the origins of the differ-

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ent types are authoritative. Gross has also given a complete résumé of the different varieties of anomaly of the gallbladder. It is suggested that confusion in the reporting of cases may be minimized by the use of some simple clinical classification, such as is indicated in Table I, which is modified somewhat from the data of Boyden and of Gross. Further, when a case of double gallbladder cannot be more accurately subclassified, as may frequently happen when roentgenographic appearance is the criterion, it would probably be wiser to call it merely "accessory gallbladder," the more general term used by Boyden in the title of his article.

There is little reason to confuse divided gallbladder and double gallbladder, since the former is practically of necessity an operative or necropsy finding, at which time the state of affairs should be clearly demonstrable. Double gallbladder, however, may be visualized by the roentgen ray alone, and it is only when the cystic ducts and their terminations can be seen (as in the present instance) that subclassification is possible. However, it is true that where there is any appreciable separation of the two gallbladders, the "H" or ductular type is probably present. Two gallbladders close together, however, may be either of the "Y" or "H" type.

Generally speaking, the divided gallbladder, or divisa type should be thought of as a single viscus with a single cystic duct. It may be in every respect of normal

TABLE I

CLASSIFICATION AND CHARACTERISTICS OF ACCESSORY GALLBLADDER

Type	Subtype	Description	Embryologic Origin
1. Divided gallbladder (Vesica fellea divisa)	a. Septate type	Septum divides cavity longitudinally more or less completely. Septum may be transverse. The loculi communicate. External appearance of gallbladder normal. One cystic duct	Incomplete resolution of solid stage of development of the gallbladder
	b. Diverticular type	Prevailing type in ungulates. Diverticulum, a sac-like protrusion, may arise from any portion of gallbladder, including fundus and neck. Diverticulum usually smaller but may be larger than main cavity and communicates with it. One cystic duct	Some, especially those near the neck, arise from persistence of cyst-hepatic ducts (ducts in embryo which pass from gallbladder bud or cystic duct into liver and normally regress). Others, especially near fundus, may be due to incomplete resolution of solid stage with pocketing off of a portion of fundus by a septum
	c. Cleft type (lobate or bifid)	Prevailing type in cats. There is division and separation of the fundic portion of gallbladder, extending to a variable degree down the body. Divisions may be unequal. Their cavities communicate with main cavity. Fundus has a lobed or bifid appearance. One cystic duct	The gallbladder primordium is partially split during the solid stage. When the viscus develops its cavity the fundic portions remain separate and may be unequal

Table I—(*continued*)

Type	Subtype	Description	Embryologic Origin
2 Double gallbladder (Vesica fellea duplex)	a. "Y" type	Two gallbladders, usually close together or adherent and occupying the same fossa. Two cystic ducts which unite to form a common cystic duct. The latter then joins the hepatic duct to form common bile duct. The gallbladders may be equal or unequal in size	Probably as an accessory outpocketing of the cystic duct "subsequent to the formation of the definitive gallbladder" rather than as a "primary subdivision of the embryonic primordium" (Boyden)
	b. "H" type (ductular type of Boyden)	Two gallbladders, completely separate, and sometimes in different lobes of the liver. Two cystic ducts. The accessory cystic duct empties independently into an hepatic duct or the common duct. The accessory vesicle may be smaller or larger than the true gallbladder	As above, except that the accessory pouching occurs in embryo from the common duct or an hepatic duct
	c. Trabecular type	Two gallbladders in the gallbladder fossa. Two cystic ducts, one of which plunges directly into the adjacent liver substance. Very rare case reported by Croudace	The accessory gallbladder arises as an outpocketing of liver cords or trabeculae bordering the gallbladder fossa and communicating with the smaller bile capillaries (Boyden)
3. Multiple gallbladder (Vesica fellea multiplex)		This has been reported in cats and ungulates. Its occurrence in humans is possible but not recorded. In this there may be three or more gallbladders, or two gallbladders with variations of the divisa type in one	

external appearance, with its cavity divided by a septum of embryologic origin (septate type); or its cavity may be bifid at the fundus (cleft type); or in communication with a diverticular pocket variously located. The double gallbladder or duplex type, on the other hand, consists of two distinct vesicles, which may be close together or quite widely separated, and two cystic ducts. The ducts terminate variously by joining (the "Y" type), by entering different parts of the extrahepatic biliary system ("H" or ductular type), or by plunging into the liver directly (the very rare trabecular type). The different forms of accessory gallbladder with their characteristics and probable embryologic origin are summarized in Table 1.

It should be noted that there is no definite evidence to indicate that the mere presence of accessory gallbladder per se predisposes to pathologic change. The anomaly may be

an incidental autopsy or roentgen finding with no sign of dysfunction. However, the anomalous organ or organs may be the seat of disease, such as inflammation, suppuration, stone, polyp, parasitization, etc. It sometimes happens that one part is diseased, another part normal; in other cases pathologic change may be present throughout but varying in type in the two gallbladders or in the divisions of one gallbladder (e.g. cases of Wilson, Scott *et al.*, Alfredo).

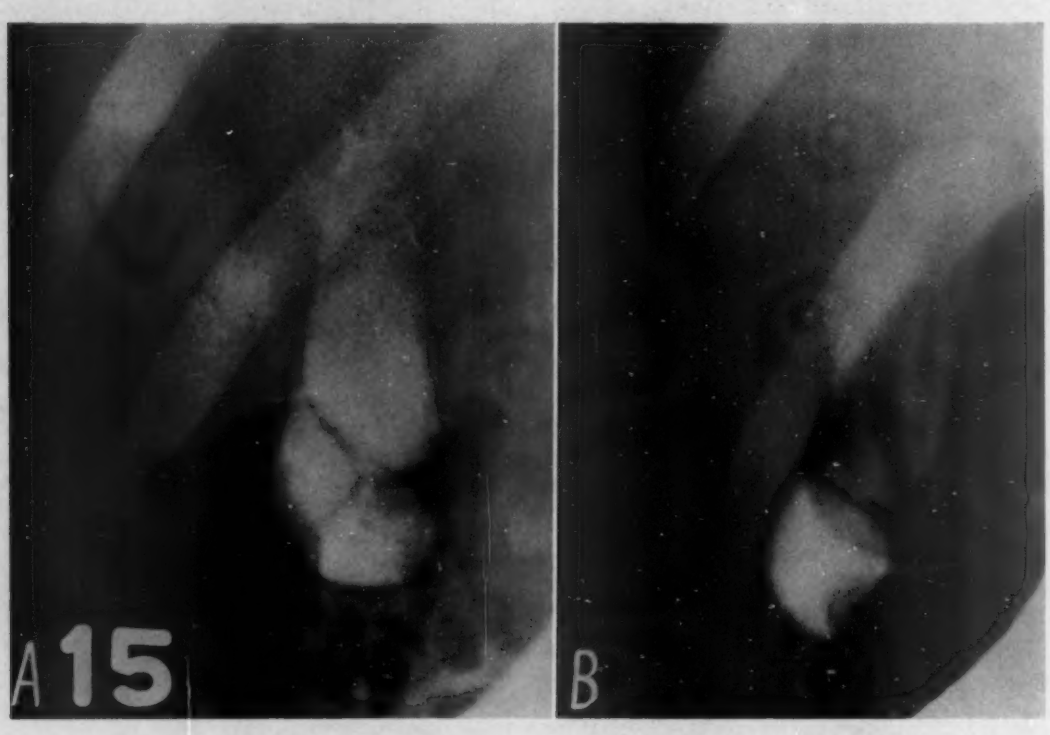

FIG. 1. Double gallbladder. Posteroanterior (*A*) and oblique (*B*) views fifteen hours after dye ingestion. The possibility of a single anomalous viscus or of deep indentation by an adhesion or band could not be excluded.

CASE REPORT

The patient, S. C., was a forty-four year old Italian welder with a ten year history suggestive of peptic ulcer and spastic colon. During the course of a complete gastrointestinal roentgen examination, cholecystography was done and the double viscus demonstrated. The gastrointestinal series showed duodenal ulcer without obstruction. In a complete study which included a period of observation and treatment in the Long Island College Hospital, there was no evidence whatever of biliary or hepatic dysfunction. There was no reason for operative interference for the ulcer symptoms responded satisfactorily to conservative treatment. The gallbladder studies were made in October, 1946. Roentgenograms taken fifteen hours after ingestion of 3 grams of priodax (Fig. 1, *A* and *B*) showed excellent dye concentration and apparently two gallbladders closely opposed, with the fundus of one lower than and partially overlapping the fundus of the other. In these views, however, one could not be certain that the appearance did not represent a single gallbladder of an anomalous type, or deeply indented by an adhesion or peritoneal band. However, roentgenograms taken after the fat meal ("cholex") were more decisive. At 15, 20, and 120 minutes (Fig. 2, *A*, *B* and *C*), two viscera were clearly outlined, one somewhat longer and narrower than the other. Two cystic ducts could be seen, joining to form a short common cystic duct,

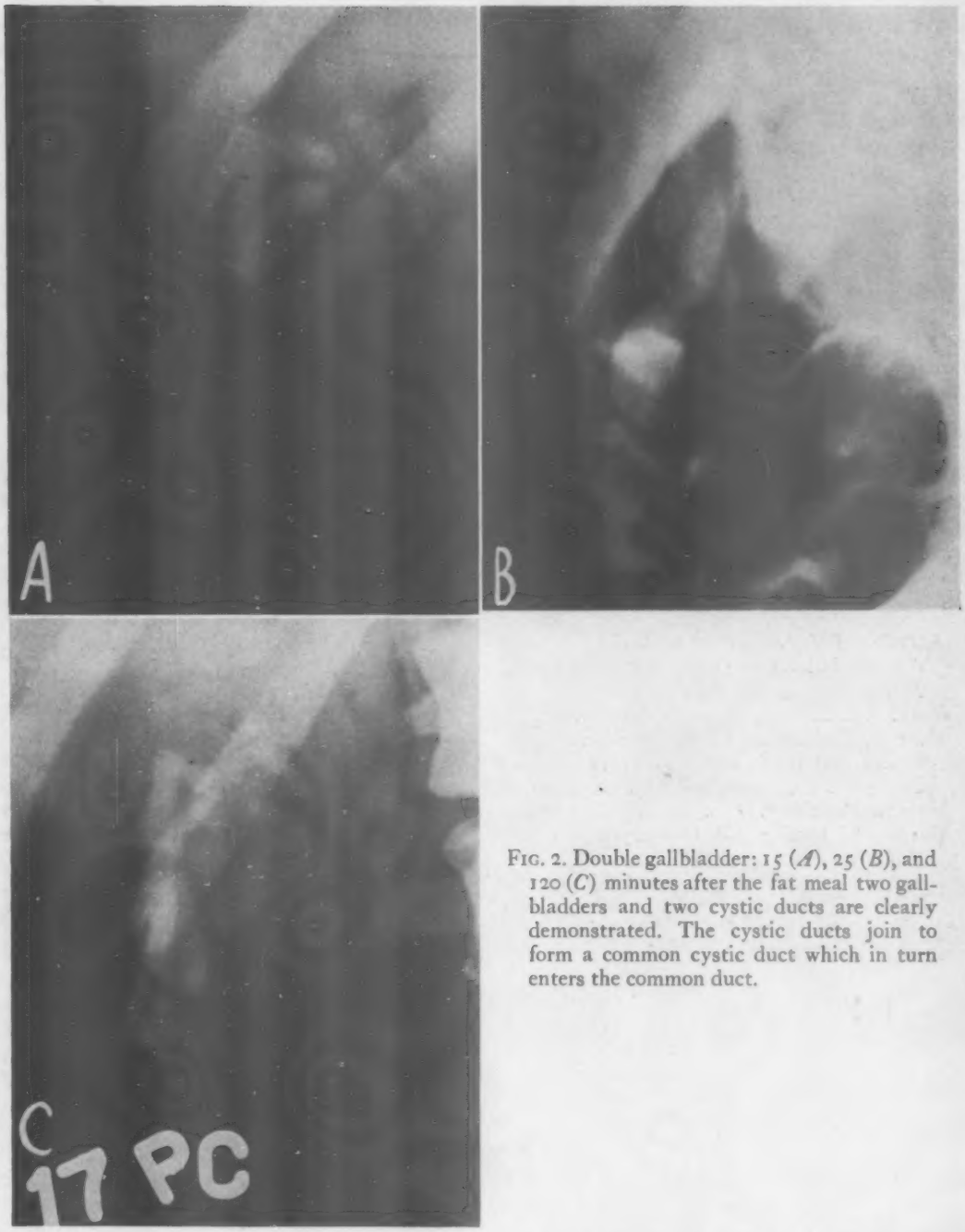

FIG. 2. Double gallbladder: 15 (*A*), 25 (*B*), and 120 (*C*) minutes after the fat meal two gallbladders and two cystic ducts are clearly demonstrated. The cystic ducts join to form a common cystic duct which in turn enters the common duct.

which in turn entered the visible common duct. A normal progressive contraction of both vesicles could be followed. There was no evidence of calculus or other pathologic process.

SUMMARY

A case of true double gallbladder (vesica fellea duplex) is reported in which for the first time there was clear roentgenographic demonstration of two cystic ducts joining to form a common cystic duct. This permitted its further subclassification into the "Y" type. A classification of accessory gallbladder of clinical value is suggested and

characteristics of the main types and subtypes summarized.

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ADDENDUM

On April 26, 1948, this patient, S. C., was subjected to gastric resection because of recurrence of his ulcer complaints. The operation was performed by Dr. Edward P. Dunn at the Long Island College Hospital. At operation the presence of two gallbladders and two cystic ducts was verified. The gallbladders were in the gallbladder fossa and had a common peritoneal investment. Further dissection and exploration of the extrahepatic biliary tract was not attempted since it would have added an unwarranted and unjustifiable risk to the major surgery required.

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CO-EXISTENT BENIGN GASTRIC ULCER AND ADENOCARCINOMA OF THE STOMACH*

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A GREAT number of articles on the pathology and surgery of the stomach are published each year but rarely is it possible to find a reference to the co-existence of benign and malignant lesions in that organ. The standard textbooks of pathology and surgery do not mention this association but certainly the incidence of this combination of lesions must be greater than a review of the literature reveals. The purpose of this paper is to present such a dual lesion.

REPORT OF CASE

The patient was a white male, aged forty-nine, whose weight had decreased about 14 pounds during the five months preceding admission to the hospital. He stated that he had vomited about once a day for the last four months, and had noticed a mild intolerance to food with a high fat content. Hematemesis and melena had not been noted. Other symptoms were completely lacking.

Physical examination was noncontributory. A mass was not felt in the abdomen.

The value for hemoglobin was 98 per cent, the complement fixation and precipitation tests for syphilis negative and the urinalysis within normal limits. Gastric analysis in the fasting state revealed a total acidity of 32 units of which 20 were free hydrochloric acid and 12 were combined. A second analysis in which histamine was used as a stimulant showed a marked response to the drug. The values for free and total acids before the administration of histamine were 6 and 18 units respectively. In one-half hour these values had risen to 50 and 80 and in one hour to 54 and 84 units respectively. At one and a half hours the values had dropped slightly to 42 and 66 units respectively. Examination of the stool revealed a one plus reaction for occult blood.

The roentgenogram of the thorax was within normal limits. Roentgenoscopic examination showed a normal appearing esophagus and the barium suspension entered the stomach in a continuous stream. The prepyloric segment of the stomach appeared constantly irregular. The duodenal cap filled out well and emptied rapidly. Serial roentgenograms of the abdomen following ingestion of the barium meal demonstrated an ulcer crater 1 cm. in diameter on the mid-portion of the lesser curvature (Fig. 1). The prepyloric segment of the stomach showed a

FIG. 1. Benign ulcer crater on mid-portion of lesser curvature of the stomach.

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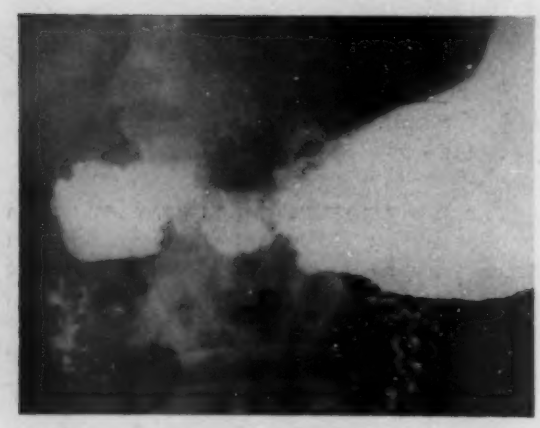

FIG. 2. Carcinoma of the prepyloric segment of the stomach.

constant irregularity (Fig. 2) and peristalsis did not pass through this area. The duodenum showed nothing unusual. The three hour film demonstrated 25 per cent gastric residue. The findings indicated the presence of a benign ulcer of the lesser curvature of the stomach and a prepyloric lesion having the appearance of a neoplasm.

Laparotomy revealed an indurated ulcer about 1 cm. in diameter on the posterior wall of the stomach near the lesser curvature at about the middle portion and a hard mass about 4 cm. in diameter in the pylorus. The regional lymph nodes lying on the head of the pancreas were firm and enlarged but gross evidence of metastasis were not found elsewhere. A subtotal gastrectomy with removal of about three-fifths of the stomach, a wide resection of the greater omentum, a dissection of the involved lymph nodes over the head of the pancreas and a wide resection of the lesser omentum were done.

The pathologic examination was made by Dr. William E. VandeGrift. The specimen was a portion of the stomach (Fig. 3), 15 cm. in length and 9 cm. in width. Two ulcers of widely divergent characteristics were present. A small ulcer, 0.5 cm. in diameter without overhanging margins, was present on the lesser curvature. Seven centimeters distal to this lesion, in the pylorus, was a second ulcer measuring 3 by 1.5 by 0.5 cm. and having firm, grayish-pink, overhanging margins. Two large lymph nodes were attached to the posterior wall of the pylorus. The larger of the two lymph nodes was 2 cm. in diameter and both nodes were almost entirely replaced by tumor tissue. One small lymph node was found in the greater omentum, but was not grossly involved by tumor.

Microscopic examination of the smaller lesion revealed a characteristic peptic ulcer inasmuch as tumor cells were not seen, the base was formed by dense scar tissue and the muscularis was drawn into the sides of the ulcer. The larger lesion was an ulcerated adenocarcinoma, the base of which was formed by granulation tissue heavily infiltrated with polymorphonuclear eosinophilic leukocytes, plasma cells, and lymphocytes. The lesion was lined internally with purulent exudate and partially digested tissue. The muscle was not drawn into the bed of the neoplasm. The tumor was seen to extend in the mucosa to a distance of 0.5 cm. from the ulcerated area but was not found in the lower portion of the muscularis or in the serosa. The involved lymph nodes were almost completely replaced by tumor similar in appearance to that found in the stomach.

The patient's postoperative period was complicated by jaundice owing to a hemolytic reaction from citrated whole blood. A slight degree of atelectasis of the lower lobe of the right lung

FIG. 3. Operative specimen showing: (*A*) benign gastric ulcer; (*B*) adenocarcinoma; (*C*) lymph nodes involved by malignant lesion.

also occurred. Both complications disappeared rapidly and the abdominal wound healed readily. The remainder of his stay was uneventful and he was discharged from the hospital on the eighteenth postoperative day.

The patient was again seen six months after operation. At that time, he stated that he felt quite well and had gained weight. Physical examination and roentgenographic examinations

of the chest and abdomen were negative for definite evidence of recurrent carcinoma or metastases.

Comment. One point of particular interest in our patient was the result of gastric analysis. Generally, it is felt that the presence of fair amounts of acid in the stomach is protection against the development or evidence for the absence of carcinoma. A casual review of the subject proves that such is not the case, for normal or even high values for hydrochloric acid do not insure benignity. This fact was likewise borne out in this particular patient.

It is noteworthy that during the roentgenoscopic examination the benign gastric ulcer was completely overlooked. The crater, however, was demonstrated on five of the serial roentgenograms. These facts illustrate the complemental value of roentgenoscopy and roentgenography in a diagnosis of small peptic ulcers. Complete reliance should not be placed in either of the examinations alone. Thorough roentgenologic study of the stomach and duodenum must include roentgenoscopic examination and routine roentgenograms made in various projections.

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ADENOCARCINOMA OF THE JEJUNUM

REPORT OF TWO CASES

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THE relative rarity of primary carcinoma of the jejunum makes worth while the reports of 2 additional cases. One was diagnosed by roentgen examination, the other was tentatively diagnosed. Review of the literature shows about three hundred cases reported. The incidence by division of the small intestine is given by Mayo and Nettrour as duodenum most frequent, ileum next and jejunum last. Shallow, Eger and Carty give the general autopsy incidence of 0.1 per cent, or 36 times less frequent than carcinoma of the colon. Three per cent of intestinal carcinomas and 60 per cent of intestinal sarcomas occur in the small intestine. Carcinoma, however, is twice as common as sarcoma.

REPORT OF CASES

Case 1. L. H., female, aged fifty-one, admitted on June 5, 1945, complaining of mild cramping pains in the abdomen for the past week. She had had nausea but no vomiting. The pain was epigastric and had been continuous since onset.

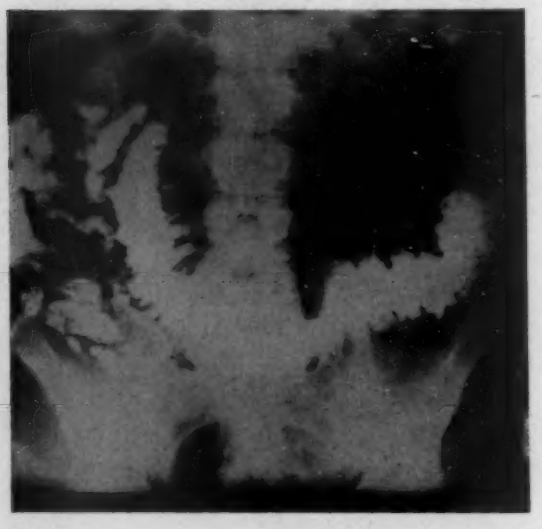

FIG. 1. Case 1. The dilated jejunal loop which presented on the first examination. Subsequent studies failed to confirm this finding.

The past history and review of systems were non-contributory.

Physical Examination. Temperature 99° F., pulse 100, respiration 20, blood pressure 260/110. The patient was an obese colored female not appearing sick and complaining only slightly of abdominal pain. The left epigastric area was the point of maximum tenderness. No mass was felt. Other positive findings were left ventricular enlargement and arteriosclerosis.

Accessory Clinical Findings. Hemoglobin, 91 per cent; erythrocyte count, 4,500,000; leukocyte count, 8,400, with polymorphonuclears 55 per cent, lymphocytes 43 per cent, monocytes 2 per cent. Urinalysis: specific gravity 1.014, reaction alkaline, negative for albumin, sugar four plus, microscopic negative. Blood sugar, 235 mg.; nonprotein nitrogen, 24 mg. per 100 cc. Wassermann reaction, four plus. The preliminary diagnosis was diabetes mellitus, syphilis, hypertension and obesity. Low grade intestinal obstruction as the cause of the cramping pain was to be ruled out.

Course in Hospital. On June 9, 1945, a gastrointestinal roentgen series was performed. The esophagus, stomach and duodenum were negative. At four hours a greatly dilated loop of jejunum was noted in the middle and lower part of the left side of the abdomen (Fig. 1). This dilatation ceased abruptly in the right lower quadrant. The caliber was twice normal. A tentative diagnosis of low grade obstruction due to tumor of the small intestine was made. An ileal roentgen series done three days later did not confirm this finding and it was felt that the abnormality noted was due to low grade obstruction which had relieved itself. Laparotomy was considered but not done because of the diabetes and syphilis. The cramping disappeared and the patient was discharged after the diabetes was brought under control.

Subsequent Course. The patient remained in good health until October, 1946 (seventeen months) at which time she developed symptoms and signs of acute intestinal obstruction. Emergency laparotomy showed a large carcinoma of the jejunum, encircling the bowel and extending well into the mesentery (Fig. 2). The lesion and involved mesentery were resected. The patient

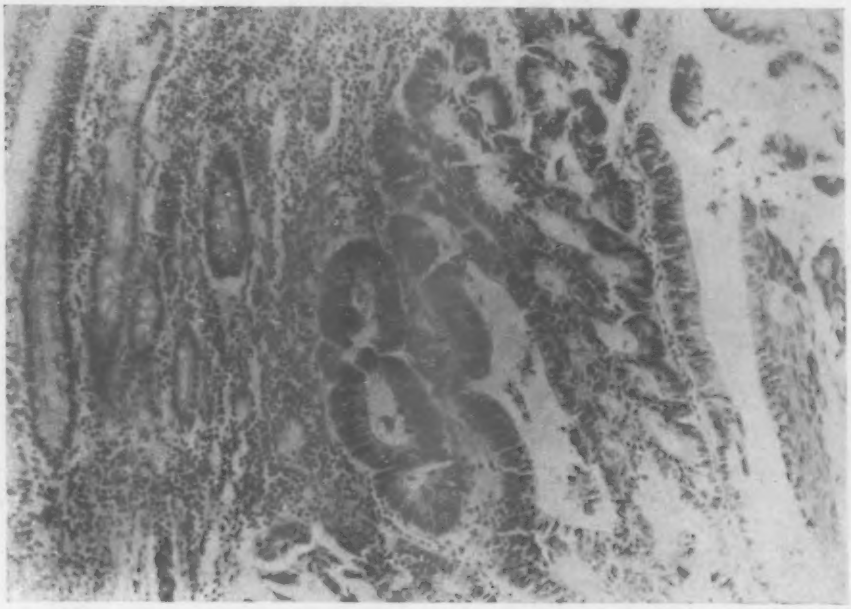

Fig. 2. Case I. Photomicrograph of the resected tumor. Adenocarcinoma.

made an uneventful recovery. She was well until April, 1947, at which time there was recurrence of the growth causing obstruction. The obstruction was relieved but the tumor could not be resected.

Case II. C. F., male, aged seventy, was admitted on January 2, 1947, complaining of pain in his stomach. The onset came one week before and consisted of colicky pain. This was followed by distention, nausea and vomiting. Past history and review of systems showed that he had had a similar attack three years before. This cleared up with bed rest. The past history was otherwise non-contributory.

Physical Examination. Temperature, 101° F.; pulse, 80; respiration, 22; blood pressure, 128/72. The patient was quite ill and complained of pain in his abdomen. He showed moderate distention but no masses were felt. Otherwise, the examination was negative.

Accessory Clinical Findings. Hemoglobin, 91 per cent; erythrocyte count, 4,760,000; leukocyte count, 7,200, with 68 per cent polymorphonuclears, and 52 per cent lymphocytes. Urinalysis: specific gravity 1.021, alkaline reaction, albumin slight trace, sugar negative.

Course in Hospital. A flat film of the abdomen showed dilated loops of small intestine and no colonic gas. The patient was treated for intestinal obstruction with parenteral fluids and Wangensteen drainage. He improved rapidly. On January 3, 1947, a barium enema examination was negative. Wangensteen drainage was continued for four days and then discontinued. He tolerated fluids well by mouth. On January 13, 1947, a gastrointestinal series showed a greatly dilated loop of jejunum in the left mid abdomen. This dilatation ceased abruptly and the distal portion of the loop was ragged (Fig.

Fig. 3. Case II. Marked jejunal dilatation with sharp and irregular narrowing of the lumen. Note that a small amount of barium has passed beyond this point.

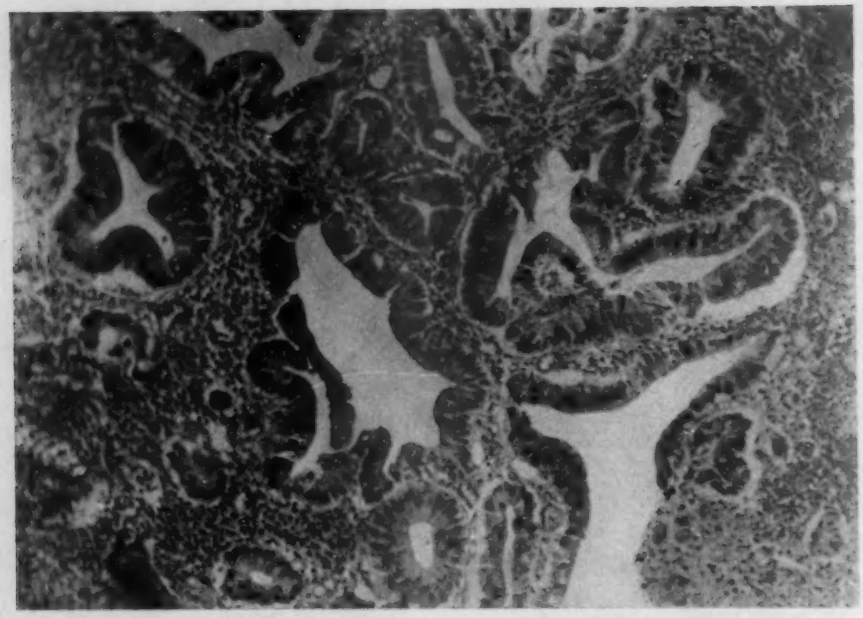

FIG. 4. Case II. Photomicrograph of the resected tumor. Adenocarcinoma.

3). A diagnosis of tumor of the jejunum was made. On January 15, 1947, a laparotomy was performed and an annular tumor found 2½ feet from the ligament of Treitz. The jejunum above was distended, below it was normal. There was no extension of the tumor. The lesion was resected with a wide margin and the abdomen closed. Histopathologic studies showed adenocarcinoma of the jejunum (Fig. 4). The postoperative course was stormy but the patient recovered after three weeks. Wangensteen drainage was maintained for one week and a secondary closure was necessary on the tenth postoperative day. He was discharged on the twenty-third postoperative day. He has been well to date.

SUMMARY

1. Two cases of adenocarcinoma of the jejunum are reported.

2. One was diagnosed preoperatively by roentgen examination, the other was diagnosed on first study but on follow-up studies the lesion could not be demonstrated.

3. It is to be noted that a tumor large enough to cause obstruction at one examination will be completely non-demonstrable subsequently.

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VOL. 61, NO. 5

THE DIAGNOSIS OF SPINAL MENINGIOMAS AND SCHWANNOMAS BY MYELOGRAPHY*

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INTRODUCTION

METHODS of accurate roentgenological diagnosis of spinal meningiomas and nerve sheath tumors have been sought, since they form the largest proportion of spinal neoplasms which can be extirpated completely by surgery. Myelography offers the best means of early diagnosis of the lesions. Almost all of the extramedullary, intradural tumors are benign neoplasms; usually meningiomas or schwannomas. Primary subarachnoidal and subdural tumors of other histopathological types are encountered infrequently.

The purpose of this paper is to point out the myelographic abnormalities which suggest the presence of a meningioma or schwannoma in the spinal intrathecal spaces.

GENERAL CONSIDERATIONS

Meningiomas, which are thought to arise from the cells covering the arachnoid villi, microscopically are composed of elongated cells in whorled arrangement. Schwannomas, which are called also neurilemmomas and neurinomas, presumably arise from the cells of the sheath of Schwann. Microscopically schwannomas consist of cells with elongated nuclei arranged side by side so as to resemble a palisade.

While meningiomas and schwannomas occasionally may be confused by gross inspection, each tumor has several growth characteristics which are helpful in differentiating the two lesions. The meningiomas are firm growths which discretely compress and angulate the spinal cord. Meningiomas, although usually subarachnoidal, are adherent to the dura over a broad surface. The schwannomas are encapsulated, soft in consistency, often cystic, and usually do not make as deep a depression in the spinal cord as meningiomas. Schwannomas usually are attached to the posterior nerve roots and rarely are adherent to the dura. As a rule the nerve sheath tumors are smoother and larger than meningiomas and may be multiple, as emphasized by Camp.[1]

Intrathecal meningiomas and schwannomas form between 60 and 70 per cent of all primary neoplasms of the vertebral canal, according to Wolf.[14] A high incidence was found also in a large number of intraspinal tumors studied by Rasmussen, Kernohan and Adson.[11] There is no large difference in the relative frequency with which spinal meningiomas and schwannomas occur. Elsberg[5] observed that 80 per cent of spinal meningiomas are seen in women and that they are more frequent in patients over forty years of age. Schwannomas occur with equal frequency in the male and female and are found as often before as after the age of forty years. Tumors of each type may grow at any vertebral level, although in the experience of Elsberg[5] over 70 per cent of spinal meningiomas were located in the thoracic vertebral canal.

ROENTGENOLOGICAL INVESTIGATION

A change in appearance of the bones in plain roentgenograms of the vertebral column is not a constant finding in patients with spinal schwannomas and meningiomas. Of a group of patients studied by Camp,[2] only 22 per cent had tumors of sufficient size to erode the vertebrae by pressure. Such bony changes were caused four times as often by schwannomas as by meningiomas. Epstein and Davidoff[7] pointed out that plain film changes are found only in advanced cases.

The value of myelography to detect in-

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traspinal tumors early has been stressed by Camp.[3] A review of the literature of myelography by Weber[13] led to the conclusion that radiopaque oils are the most satisfactory contrast media for study of the subarachnoid space. Camp[3] stated that today the procedure has attained a high degree of accuracy for the detection and localization of a tumor that is equalled by few other diagnostic roentgenological methods.

The use of myelography in the past has been limited to the demonstration of the tumor and the identification of its vertebral level. A definite diagnosis of meningioma or schwannoma has been made only in isolated instances or in small groups of patients, such as the observations of Reiser,[12] Peiper,[9,10] Odin, Runström and Lindblom[8] and more recently of Epstein and Davidoff.[7] Perhaps the largest group of patients with tumors studied by myelography was reported by Camp.[2] An analysis of the myelogram abnormalities of a group of patients studied at the Neurological Institute indicates that a benign extramedullary, intrathecal tumor can be diagnosed by the radiologist in almost every case in which such a lesion is present.

MATERIAL

Thirty cases of intradural spinal meningiomas and nerve sheath tumors studied by radiopaque oil myelography have been reviewed. In each instance the tumor was removed surgically. The tumors were classified by histopathological examination of the specimen.

Meningiomas and schwannomas occurred with almost equal frequency. There were 16 patients with tumors of meningeal origin and 14 patients with nerve sheath tumors. More women than men had tumors of each type; 70 per cent of the meningiomas occurred in women. Sixty-three per cent of the meningiomas were found in the thoracic region (Table 1).

The average age of the patients with meningiomas was forty-nine years. Only 2 patients were below the age of forty years; the youngest was thirty-seven years of age. The average age of the patients with schwannomas was thirty-eight years. There were almost as many patients below the age of forty years as above; the youngest patient was fifteen years old.

A study of the myelography films of the 30 patients disclosed that in every case an obstruction to the flow of radiopaque medium occurred at the upper or lower margin of the tumor. A part of each tumor was outlined sharply at the point of obstruction because of close contact of the radiopaque medium with the mass. In some instances, the obstruction was incomplete and in such myelograms the tumor was outlined on more than one side (Fig. 1, 2, and 4).

Table I

Analysis of 30 cases of spinal meningiomas and schwannomas

	Both Types	Meningiomas	Schwannomas
Male	11	5	6
Female	19	11	8
Over 40 years of age	22	14	8
Under 40 years of age	8	2	6
Average age (years)	44	49	38
Bone changes in plain films	5	2	3
Complete obstruction to radiopaque oil flow	20	11	9
Incomplete obstruction to radiopaque oil flow	10	5	5
Cervical tumors	7	3	4
Thoracic tumors	15	10	5
Spinal cord displaced	22	13	9
Lumbar tumors	8	3	5
Cauda equina displaced	6	2	4
Cauda equina not displaced	2	1	1

The outline of the tumor usually appeared as a concave filling defect in the head of the column of radiopaque oil. The margins of the lesions appeared smooth except at points of attachment to the meninges. In each case the tumor grew more to one side of the midline than the other so that it could be designated as predominantly right lateral or left lateral in position from the frontal roentgenogram.

The majority of the tumors occurred

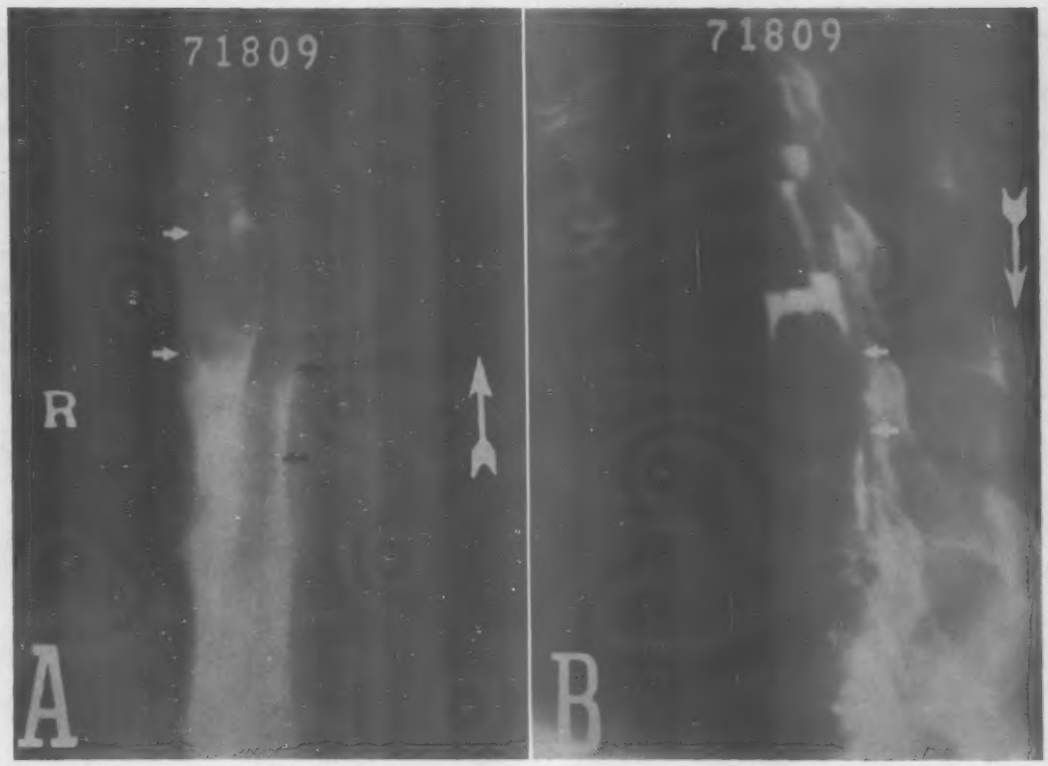

FIG. 1, *A* and *B*. Meningioma at T-7. (Note: The large vertical white arrow in this and subsequent illustrations indicates the direction of gravitational flow of the radiopaque oil column at the time the myelogram film was made.)

A fifty-four year old woman (Unit No. 870914) entered the hospital because of pain in the right flank and right lower extremity. She was unable to walk for six months before admission. The patient had a spastic paraplegia. Sensibility to all stimuli was diminished below the ninth spinal cord segment. The cerebrospinal fluid contained 162 mg. per cent protein.

An almost complete obstruction to the cephalad flow of radiopaque oil was found at T-7 when myelography was performed. A filling defect (white arrows) in the contrast medium, caused by an oval tumor attached to the dura on the right side over a wide area, was demonstrated (*A*). The spinal cord, indicated by a band of diminished density (black arrows), was displaced to the left. A small amount of radiopaque oil, which passed cephalad between the tumor and spinal cord, outlined the upper margin of the mass when the patient was placed upright. A lateral film (*B*), with the patient erect, showed that the contrast medium did not pass behind the tumor, which suggested that the mass was adherent also posteriorly to the dura over the area between the arrows. At operation a meningioma, attached to the inner surface of the dura, was disclosed behind and to the right of the spinal cord.

above the level of the first lumbar vertebra, the level of the lower end of the spinal cord. Three meningiomas were in the cervical region, 10 in the thoracic region and 3 meningiomas were at lumbar levels. Four schwannomas were found in the cervical vertebral canal, 5 in the thoracic, and 5 in the lumbar region. In all of the cases with tumors at spinal cord levels the margins of the spinal cord were outlined and the spinal cord was found to be displaced lateralward and compressed by the tumor (Fig. 1, 2, 4, and 5). Ventral or dorsal displacement of the spinal cord by the tumor was revealed in some cases in which satisfactory lateral myelograms were obtained.

In 8 patients the tumor was located below the lower end of the spinal cord. In 6 of the 8 cases the roentgenograms showed the outline of spinal nerve roots displaced lateralward by a neoplasm (Fig. 3 and 6).

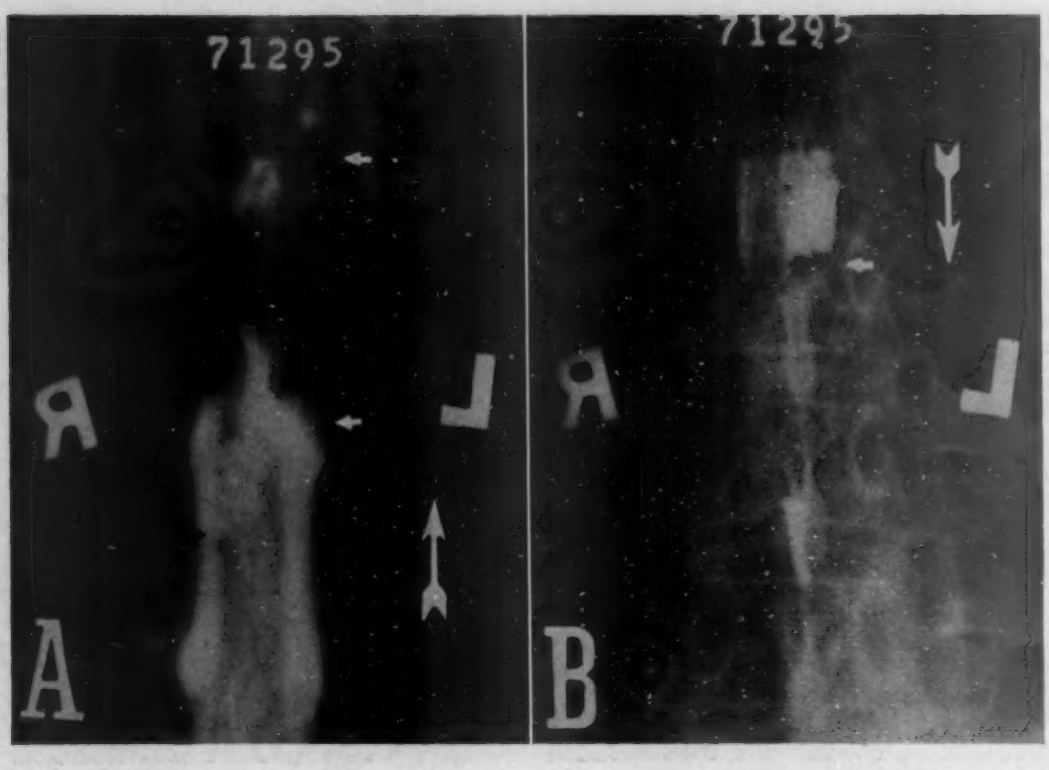

Fig. 2, *A* and *B*. Meningioma at T-8. A fifty-two year old woman (Unit No. 865071) was admitted to the hospital because of pain in both knees which had been present for three years. Both legs were described as being stiff and for one year she had unsteadiness on walking. The patient had a spastic gait with dragging of the toes of the left foot. There was questionable slight impairment of touch and pain sensation below the level of the tenth thoracic spinal cord segment.

Myelographic examination revealed an incomplete obstruction to the cephalad flow of radiopaque oil at the level of T-8. The irregular lower and medial margins of a tumor (white arrows) were outlined on the left side of the subarachnoid space by the head of the oil column (*A*). The spinal cord (black arrows) was displaced to the right and compressed. A small amount of contrast medium, which passed into the upper thoracic region, outlined the upper margin of the tumor (white arrow) at the lower margin of T-7 when the patient was placed erect (*B*). After a laminectomy was performed, an intrathecal meningioma was found extending around two-thirds the circumference of the spinal cord on the left side.

Two patients, in whom the myelogram failed to show displaced nerve roots, had very large tumors. Marked distortion of normal structures was found at the time of operation in the 2 cases; in 1 instance nerve roots could not be identified by the surgeon on gross inspection of the lesion at the operating table.

COMMENT

A sharply outlined defect in the advancing head of the radiopaque oil column at myelography was recognized by early investigators as a roentgenological characteristic of intradural tumors. The ability to differentiate obstructing intradural tumors from extradural lesions has been denied recently by Epstein and Davidoff.[6] Camp and Addington[4] stated that in approximately 20 per cent of patients it was not possible to determine the relationship of a spinal tumor to the meninges and spinal cord. A clearly defined tumor margin, indicating an intradural lesion, was observed in the myelograms of all of the 30 patients in the group which has been discussed.

The importance of displacement of the spinal cord and spinal nerve roots as evidence of an extramedullary lesion previously has not been emphasized. Early stu-

dents of myelography believed that extramedullary lesions should displace the spinal cord. Odin, Runström and Lindblom[8] observed in 1 patient at myelography a displaced spinal cord due to a thoracic meningioma.

Twenty-two patients of the group under consideration here had tumors at some level

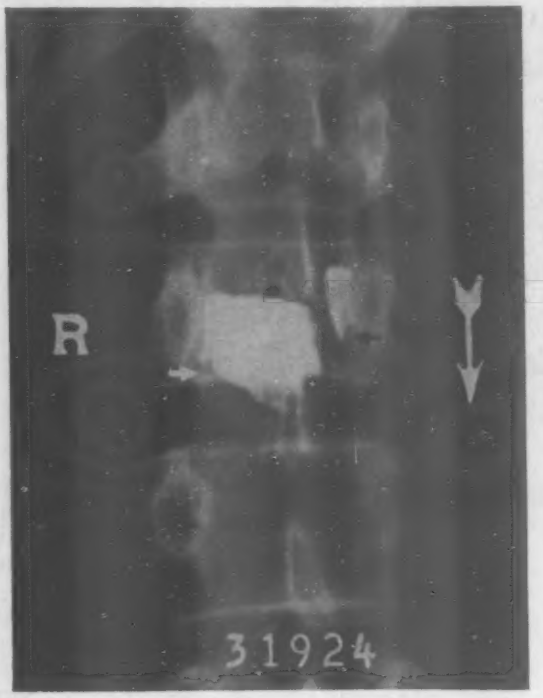

Fig. 3. Meningioma at L-3. A thirty-nine year old woman (Unit No. 589483) had pain in the lower back for two years. Nine months before entering the hospital the patient developed severe pain in the right hip and thigh. There was progressive weakness of the right lower extremity. The patient had atrophy of the muscles of the right thigh and leg. The deep tendon reflexes of the right lower extremity were inactive. Areas of hypesthesia and hypalgesia were present in the right leg.

Myelography disclosed an obstruction to the caudad flow of radiopaque oil at L-2/3. The upper margin of a mass (white arrow) was outlined distinctly on the right side of the subarachnoid space. A large spinal nerve root (black arrow) was shown displaced to the left by the tumor. At operation a large intra-arachnoidal meningioma, measuring 2.5 cm. in length and 1.5 cm. in diameter, was found. The neoplasm was attached to the right dorsal part of the dura. One swollen nerve root passed over the top of the tumor on the left side.

Fig. 4. Schwannoma at C-7/T-1. A fifty-one year old housewife (Unit No. 850123) was admitted to the hospital because of pain in the upper back for four years. For fifteen months she had stiffness and weakness of the legs. Paresthesias of each hand, which were more severe on the hypothenar side, were experienced for several months. The patient had a spastic paraplegia. Pain sensation was diminished below the second thoracic dermatome and temperature sensation was impaired in each leg and foot.

Myelography disclosed delay in the cephalad passage of oil at the C-7/T-1 level. Here the oil passed slowly around a tumor, flowing chiefly along the left side of the subarachnoid space. When the patient was tilted upright a spherical discrete mass (white arrows), apparently unattached to the meninges, was encompassed by the subarachnoid column of radiopaque oil. The spinal cord (black arrows) was displaced to the left and compressed by the tumor. At operation an encapsulated schwannoma was disclosed on the right ventral aspect of the spinal cord.

of the spinal cord. In each instance displacement of the spinal cord by the tumor was demonstrated by myelography. Cau-

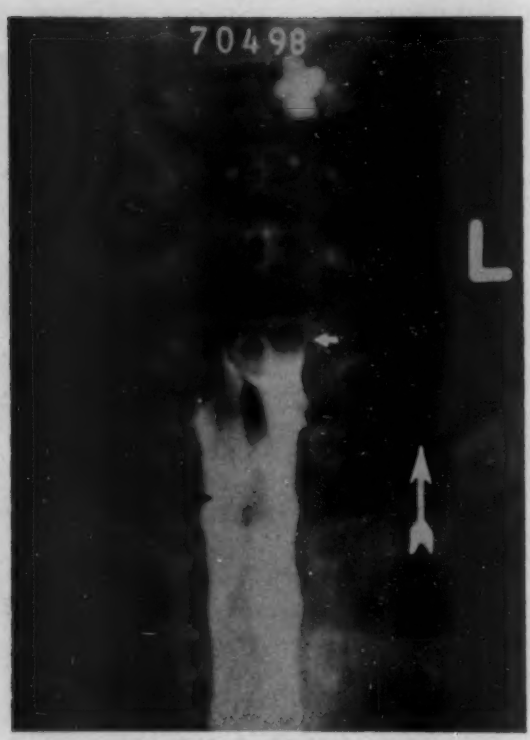

Fig. 5. Schwannoma at C-7/T-1. A forty-seven year old housewife (Unit No. 857320) complained of paresthesias of the left forearm and hand of two years' duration. Four months before admission to the hospital she had sudden onset of pain in the upper back, left side of the neck, left shoulder and left upper arm. For one month the right leg was weak and she had no vesical sphincter control. The patient had hypotonia of the muscles of the left arm and almost complete paralysis of both legs. A level of impaired sensation for touch, pain and temperature stimuli was established at the second thoracic dermatome.

Myelographic examination disclosed an incomplete obstruction to the cephalad flow of contrast medium at the level of T-1. The lower margin of a smooth, discrete intrathecal mass (white arrow) was outlined on the left side at this level. A small amount of radiopaque oil passed along both the lateral and medial sides of the tumor to the upper cervical region. The spinal cord (black arrows) was displaced sharply to the right and compressed by the tumor. At operation an oval intradural schwannoma, attached to a nerve root on the left dorsal aspect of the spinal cord, was disclosed.

dad to the conus medullaris the demonstration of displacement of spinal nerve roots was found to be of diagnostic value in differentiating meningiomas and schwannomas from tumors of intramedullary origin. Camp[3] attempted only the differentiation

Fig. 6. Schwannoma of the cauda equina. An eighteen year old stenographer (Unit No. 3024-H) complained of pain in the right thigh of nine months' duration, especially on changing position, coughing, sneezing or laughing. The pain gradually increased in severity until walking became very painful. The patient had atrophy of the muscles of the right thigh. The deep tendon reflexes of the right lower extremity were absent.

Roentgenographic examination of the spinal subarachnoid space, after the injection of radiopaque oil, disclosed a complete obstruction to the caudad flow of contrast medium at the L-2 level. The lower end of the radiopaque column outlined the upper margin of a large smooth tumor (white arrow) in the right side of the lumbar subarachnoid space. Linear radiolucent filling defects (black arrow) in the contrast medium, which were thought to represent displaced filaments of the cauda equina, were demonstrated on the left side. A laminectomy was performed from L-1 to L-3 and the dural and arachnoidal membranes were opened. An oval schwannoma, which measured 3 cm. in length and 2 cm. in diameter, was attached to the right second lumbar nerve root. The cauda equina was situated far to the left of its usual position.

of extradural from intradural lesions in this region.

The preoperative differentiation of meningiomas from schwannomas is of more academic than practical interest, since tumors of both types usually are amenable to complete surgical excision. In several of the 30 cases reviewed a meningioma rather than a schwannoma was suspected because the myelogram disclosed a tumor with a broad meningeal attachment and slightly irregular surface (Fig. 1 and 2). A schwannoma was considered the more likely type of neoplasm when the radiopaque medium surrounded an encapsulated mass (Fig. 4).

SUMMARY

1. A review of the myelograms of 30 patients with intradural spinal meningiomas and schwannomas revealed that a partial or complete obstruction to the flow of contrast medium by the tumor occurred in every case. Each neoplasm produced a sharply demarcated filling defect in the radiopaque oil column indicative of an intrathecal tumor.

2. In 28 patients displacement of the spinal cord or spinal nerve roots by the neoplasm was demonstrated in the myelogram. Displacement of these nerve structures signifies that the lesion is extramedullary.

3. A meningioma rather than a schwannoma may be suspected when the myelogram discloses a tumor with a broad dural attachment and slightly irregular surface. Schwannomas, being encapsulated, are surrounded by the radiopaque oil more thoroughly than meningiomas.

4. The correct diagnosis of spinal meningioma or schwannoma may be made at myelography by the radiologist in almost every case in which such a lesion exists. It is important that these tumors be recognized since they can be extirpated completely by surgery.

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OSTEOGENESIS IMPERFECTA TARDA

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OSTEOGENESIS imperfecta is a disorder of bone formation in which increased fragility of the bone is the most important manifestation. There was once a tendency to differentiate as different diseases an infantile or congential form, which was called osteogenesis imperfecta, and another type found in childhood and adolescence previously called fragilitis ossium, but which is now classified as osteogenesis imperfecta *tarda*. Most modern workers include both illnesses as a variety of the same disease. Our experience leads us to the same conclusion. A complete classification modified from Knaggs'[8] excellent study follows:

Classification of Osteogenesis Imperfecta

I. Fetal Variety.
   1. Stillborn or lives a short time only.
   2. Numerous fractures of the ribs and long bones are found.
   3. Skull ossification is incomplete, the skull often being only a membranous bag.

II. Infantile Variety
   1. Less severe than fetal type.
   2. May continue for several years, although the prognosis is still poor.
   3. Ossification of cranium incomplete, but much further advanced than fetal type.

III. Osteogenesis Imperfecta Tarda or Fragilitas Ossium.
   1. Infant is born healthy and may have a normal childhood except for fractures occurring from the slightest cause. These fractures may begin at birth or shortly thereafter.
   2. As patient grows older, there is often less tendency for fractures to occur.
   3. Associated findings:
      Blue sclera
      Deafness of otosclerotic type
      Peculiar shape of the skull
      Laxity of ligaments
      Abnormality of the teeth, nails or hair
      Shortened length of long bones
   4. Findings may vary in each case.

The characteristics of each type are not clear cut or mutually exclusive. The adult patient in our series is definitely of the tarda type and the child is undoubtedly of the tarda type. The skull ossification of the child patient was complete.

The most characteristic evidence of osteogenesis imperfecta is the bone fragility resulting in an extremely large number of fractures caused by the slightest possible trauma. This symptom and others that will be detailed below are inherited, and this inheritance follows usually a "dominant" pattern[14]. About one-half of a generation is affected, and the transmission is generally "direct," i.e., a parent affected with this disease transmits the abnormality to half of his or her progeny, and the half that escape do not transmit the condition to their offspring. There are probably exceptions to this rule. In a very few cases, heredity does not seem to be a factor, but enough generations may not have been studied, because the defect can conceivably skip one or two generations. There is no sex-linkage of the trait, nor is there a preponderance of one sex over the other with this defect.

In addition to the brittleness of the bones there are several other characteristics that may or may not be found in a fully developed case. These are china blue coloration of the sclera, deafness of the otosclerotic type and hypermobility of the joints. Even in those children who do not inherit the bone fragility, the blue sclerae and a peculiar brownish colora-

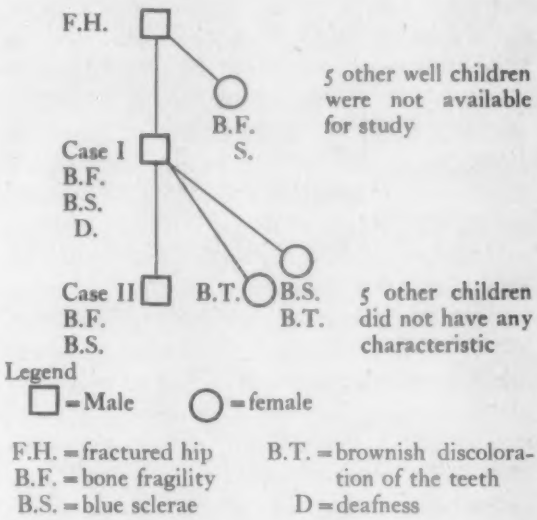
tion of the teeth may be found. The coloration of the sclera is due to a deficiency of the quality or quantity of the fibrous tissue of the sclera, thus permitting the dark pigment of the choroid to shine through. The brownish discoloration of the teeth is more than likely due to a transluency of the enamel.

The blue sclera, even though it is an innocuous symptom, is an important characteristic of osteogenesis imperfecta, because in a thorough review of the literature, Fraser was unable to find even one case of bone fragility in osteogenesis imperfecta with a white sclera.

The peculiar shape of the skull is another characteristic in this disease. It resembles an inverted triangle with the base of the triangle representing the top of the skull. The forehead is broad and bulges forward, and the parietal bones bulge over the external auditory meati, pushing the ears down and out. The cause of this peculiar deformity is unknown but one authority believes that it is due to the lack of support given to the developing brain by the soft cranium.

Twenty-five per cent of the patients with osteogenesis imperfecta develop deafness, that has been shown to be due to otosclerosis. This symptom usually appears after twenty-five years of age, when the tendency to bone fragility has waned. When this point has been reached, the patient will often boast how tough his bones are, and how he now is able to do things he formerly dared not do.

The family tree of our patients is shown in the next column.



ETIOLOGY

The etiology of osteogenesis imperfecta is unknown. Key believes that this disorder is due to congenital instability of the mesenchyme or a hereditary hypoplasia of the mesenchyme. According to Arey's[1] excellent manual of embryology, "Developmental Anatomy," the mesoderm, one of the three primary germ layers forms the mesothelium and the mesenchyme. The mesothelium differentiates into the pericardium, pleura, peritoneum, urogenital epithelium and striated muscle. The mesenchyme differentiates into smooth muscle; notochord (which forms part of the vertebral column), connective tissue, cartilage, bone, blood, endothelium of the blood vessels, lymphoid organs and the suprarenal cortex. The sclera of the eye is also formed from the mesenchyme.

Some of the signs of this condition can be explained by a mesenchymal hypoplasia while others cannot. Bone fragility, bluish discoloration of the sclera, and laxity or hypermobility of the joints can thus be accounted for, but we cannot attribute the brownish discoloration of the teeth to this cause, because the enamel of the teeth comes from the ectoderm. Some of the patients show a defect of the nails which is also an ectodermal structure. Many of these patients also show blue tympanic membranes. One of our patients (Case 1) showed this phenomenon. The tympanic membrane is formed from the three germ layers. The central portion is mesodermal while the internal portion is endodermal and the external portion is ectodermal. Thus if an analogy is drawn with the blue sclerae, the defect is in the diminution of thickness of the ectodermal layer allowing the color

of the mesodermal layer to shine through. Thus it seems that there is more than one germ layer involved, i.e. certainly two and perhaps all three layers.

Some investigators[17,18] suspect a faulty metabolism resulting from various endocrine disturbances to be the underlying defect in osteogenesis imperfecta. However, at autopsy, the entire system of ductless glands has been found to be structurally normal. On the other hand, Rosenbaum[18] cites the literature to show that bone fragility may be due to an alteration in the region of the anterior pituitary gland. According to his view, decalcification of the skeleton sometimes follows cerebral disorders. We noted a case in the literature of fragility of bone associated with an hypophyseal tumor. Rosenbaum recommends that these patients be treated with anterior pituitary hormone. While the possibility that the cause of osteogenesis imperfecta is due to pituitary gland dysfunction is an attractive theory, it does not have sufficient evidence to support it. One of our patients (Case 1) has an intractable bleeding peptic ulcer. This might possibly support the pituitary dysfunction theory, since in 1932 Cushing[3] noted that functional derangement of autonomic centers in the hypothalamus may play some part in the causation of peptic ulcer. However, more recent work seems to lean toward the theory that acute gastric erosions may result from this derangement of function, but not chronic peptic ulcer.

HISTOPATHOLOGY AND PATHOGENESIS

The pathogenesis of this condition is unknown and various authors have given their individual opinions on this subject.

To discuss the complicated process of normal bone formation is outside the scope of this paper. However, it might not be amiss to list certain salient features, so that the process of abnormal bone production can be understood.[9] Normal bones are not transmuted or indurated cartilages, but are new formations, produced around or within the cartilage which are later destroyed. Certain bones (flat bones of the skull) are produced from connective tissue directly without having been preformed in cartilage. These are called membrane bones in contradistinction to cartilage bones.

Bone is formed both around the cartilage (perichondrial bone) and within the cartilage (endochondrial bone), and the cartilage itself degenerates. The typical long bone of the adult consists of (1) periosteum, (2) a laminated area forming the haversian canals which surround the nutrient blood vessels, and (3) the marrow cavity. The bone cells are situated between the lamellae or layers of bone. Each haversian system consists of an artery and a vein and is surrounded by concentric lamellae of bone. Between these lamellae the bone cells are found. All the bone cells of the haversian system receive nutriment through the canaliculi opening into the central canal in which the artery and vein are situated. Knaggs[8] believes that there occurs in osteogenesis imperfecta a metaplasia of cartilage cells directly to abnormal bone cells. These abnormal bone cells are large and oval and show no tendency to form canaliculi. The new bone is imperfectly laminated and sometimes even granular. From this property the synonym of this disease "osteopsathyrosis," has been introduced.

At the epiphyseal line there is no abnormality in the zones of cartilage proliferation and calcification. However, there is a failure in the next stage, in that there is no invasion of the calcified cartilage by the osteoblasts of the marrow. Instead the calcified tissues seem to undergo a process of metaplasia into abnormal bone, the cartilage cells appearing to become the new abnormal bone cells. This new bone forms slender, delicate, longitudinal trabeculae with large interstices filled with delicate connective tissue or fibrous marrow.

The shortened length of the long bones may be due to the interference with the normal processes of bone formation at this part of the epiphyseal line.

The bone formed by the periosteum is also abnormal. The fibrous periosteum

is thicker than usual and the bone cells in its deep surface are large and oval, closely resembling cartilage cells. Knaggs believes that they are true cartilage cells. New bone is formed by calcification and ossification around these abnormal cells. The new bone is said to be non-laminated, has no haversian canals, and is granular and porous, with numerous spaces filled with loose connective tissue. The cortex of the bone is thin. These changes impair the strength of the shaft and lead to increased fragility.

MacCallum[12] agrees with these findings for the most part, except that he does not recognize the direct metaplasia of the cartilage cell to the abnormal bone cell.

Loesche[10] finds that these cases have a sufficient number of osteoblasts, but he feels that they are functionally inefficient and that this disease is due to the lack of capacity of osteoblasts to form osteoid tissue.

There seems to be some difference of opinion by different authorities as to whether the bones are hard or soft. Fraser[4] in discussing biopsy of bone in patients with this condition comments on the extreme density and hardness of the bone and states that the bone feels and cuts like marble. Lutz[11] states that the bones are usually soft. Undoubtedly they are speaking of the two different stages of this condition, the former about the end stage when the tendency to fragility has been lost, and the latter when the marked fragility is still present.

ROENTGENOLOGICAL STUDIES

The roentgenological picture varies according to the type of the disease.[11]

In the fetal type, there is marked acalcification of all the bones. There are numerous fractures of the long bones. The ribs and skull show small, thin isolated plates of bone.

The infantile type presents similar, but less pronounced findings.

In the delayed type, i.e., osteogenesis imperfecta tarda, there are many evidences of old ununited fractures, marked bowing of the long bones and acalcification. The cortex of the long bones is thin. The translucent roentgen shadows with the attenuated trabeculae are the typical appearance of the bones. Some of the authorities have noted the slender shaft and the expanded extremities of the bones.

In the healing of the fractures, the callus in some of the cases seems to be minimal, while in the others, the callus is exuberant. In our patients the bone was markedly thickened at the fracture site following healing. As a result of this thickening, the bone appeared to be bowed at this level.

DIFFERENTIAL DIAGNOSIS

In infants and young children, osteogenesis imperfecta must be distinguished from rickets, congenital syphilis and scurvy. The normal epiphyseal lines as seen on the roentgenogram in osteogenesis imperfecta serve to exclude the other conditions.

The roentgen characteristics of the condition would also exclude bone tumors and osteitis fibrosa cystica. In osteogenesis imperfecta the blood calcium, phosphorus and alkaline phosphatase are normal, while in osteitis fibrosa cystica, the blood calcium is elevated, the phosphorus is depressed and the alkaline phosphatase is usually increased. Some authors state that the blood alkaline phosphatase is increased also in osteogenesis imperfecta, but the consensus now is that this finding is within the normal range. This was true of our cases.

The differential diagnosis from osteomalacia is somewhat more difficult. Osteomalacia is usually found in pregnant women and in this condition the bones usually bend rather than fracture. In osteomalacia the bone trabeculae are made up of osteoid tissue and general lack of calcuim deposit. In osteogenesis imperfecta, since there is failure of proper evolution of the osteoblast, there is defective bone formation. It is said that this distinction can be made from a biopsy specimen. We have had no experience with biopsy in these diseases.

FIG. 1. Photograph of Case 1, illustrating the large parietal bosses, eversion of the ears and the tendency of the skull to appear like an inverted triangle.

TREATMENT

The treatment in this condition has been haphazard, as would be expected from the fact that both the etiology and pathogenesis are unknown. However, some experimental therapeutic trials warrant further investigation.

Viosterol and parathyroid extract appear to be contraindicated in this condition according to Hansen.[5,6] Both of these substances cause an increased output of calcium and phosphorus to the extent that a negative calcium balance is produced. This finding occurs following treatment in patients with osteogenesis imperfecta as well as in normal persons. In cases of osteogenesis imperfecta without treatment, Hansen also found a negative calcium balance, so that the administration of viosterol or parathormone would accentuate a disturbance already present.

Experimentally, it was found that if the thymus was removed, induced fractures were slow in uniting. For this reason, Ryan[15] and Secord *et al.*[16] fed thymus gland extract to a patient with this disease and reported good results.

Chess, Chess and Keeton[2] advised giving these patients testosterone and noted an improvement in general appearance and increased vigor in one patient with osteogenesis imperfecta. His patient had before treatment a negative calcium, phosphorus and nitrogen balance and a low blood calcium, phosphorus and alkaline phosphatase. After treatment there developed a positive calcium, phosphorus and nitrogen balance with essentially normal figures for these substances.

Rosenbaum[18] suggested treatment with anterior pituitary hormone because of reasons discussed above under the heading of "Etiology."

Certainly the fact that these patients improve as they approach adulthood seems to suggest that an endocrine gland may be

FIG. 2. Roentgenogram of skull of Case 1, showing the forehead bulging forward.

involved as the cause of the improvement. Since nothing else can be done for these unfortunate people anterior pituitary-like hormone or testosterone should be tried.

On reviewing the history of these patients one is impressed by the remarkable number of accidents that these patients have. However, this impression seems to be more apparent than real. The "accidents" that cause frequent fractures in these patients are experienced by most of us without undue effects of any kind.

CASE REPORTS

Case 1. J. LaD., Sr., male, aged forty-six, had a history of recurring fractures caused by slight traumas, recent onset of deafness, and in recent years recurrent episodes of bleeding peptic ulcer. At the age of eight, he fractured his left patella when he jumped off a wagon. At fourteen years of age he fractured his left femur and left arm because of a slight fall. Between fourteen and seventeen years of age, his left forearm was fractured five or six times, when he fell from a horse, when he was struck by a baseball

Fig. 3. Roentgenogram of one of the femurs of Case 1, showing bowing of the femur and thickening of the bone at one of the fracture sites.

Fig. 4. Case 1. Separation of acromioclavicular junction.

Fig. 5. Case 1. The deformity of the antral portion of the stomach and the duodenum is shown.

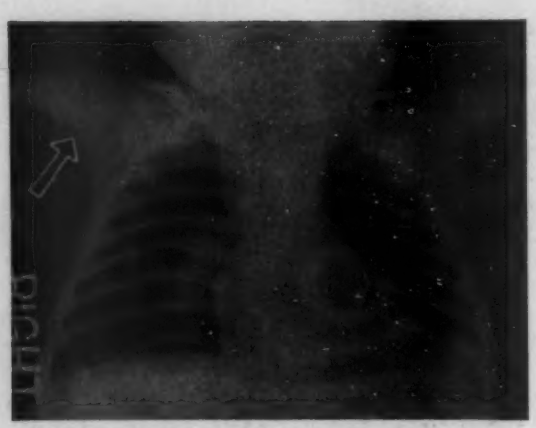


FIG. 6. Case II. Arrow indicates separation of the head from the neck of the humerus at birth.

and when he fell several times while playing. At twenty years of age he dislocated and fractured his left hip when he tripped while stepping from a curb. At twenty-seven years of age, he had a possible fracture of the skull when he fell from a motorcycle. Again in this year, he fractured his right femur when he was struck by an elevator door. At thirty-four years of age, he fractured the two bones of his shoulder girdle when he fell from a slowly moving car. At thirty-eight years of age, he fractured the two bones of his right shoulder girdle when he fell down ten steps.

At thirty-three years of age he first gave a history of having pains in the epigastric region that were relieved by food. At forty-one years of age, he was hospitalized for bleeding peptic ulcer. He gave a typical history of epigastric pain with relief by food or vomiting. A gastrointestinal roentgen series revealed marked hypertrophy of the stomach and a persistent irregularity of the duodenal bulb. At the time of this admission to the hospital, he had no pain, but had experienced faintness and had noticed that he had jet black stools.

At forty-two years of age he was again admitted to the hospital for epigastric pain. A gastrointestinal roentgen series showed persistent narrowing in the prepyloric region of the stomach and an irregular duodenal cap. The blood chemistry was as follows: Urea 26 mg., glucose 67 mg., calcium 11 mg., phosphorus 3.3 mg., per 100 cc. of blood. At another time the blood chemistry report was: glucose 57 mg., calcium 9.35 mg., phosphorus 3.0 mg., per 100 cc. of blood. A repeat determination of the blood sugar showed it to be 69 mg. per 100 cc. of blood.

Later that year he was again hospitalized for bleeding peptic ulcer. His symptoms on admission were dizzy spells and jet black stools. The calcium content of the blood was 10.8 mg., phosphorus 2.9 mg., albumin 5 mg., globulin 2.52 mg., per 100 cc. of blood. The alkaline phosphatase was 6.0 units and the acid phosphatase was 2.25 units.

At forty-five years of age, he again had tarry stools and vomited slightly. Clots were found in the vomitus. It was noted at this admission that he presented a bluish discoloration of the sclerae and a moderate amount of deafness, as well as a deformation of most of the bones in his body. The peculiar inverted triangular shape of his skull was also noted. He was blind in his right eye, which he said was due to one of his accidents. Examination revealed an optic atrophy, but the optic nerve had appeared to be bluish-white instead of a dead-white. His ears showed bluish tympanic membranes.

A gastroscopy done by one of us (L.P.) revealed a normal stomach. The gastrointestinal roentgen series showed an irregular duodenal cap. The hemoglobin was 60 per cent, the red blood cell count was 3.44 million, the white

FIG. 7. Case II. Fracture of the femur with callus formation is shown.

blood cell count was 12,400, with 83 per cent polymorphonuclear cells. The blood was Rh positive. The blood chemistry was as follows: urea 53 mg., creatinine 1.9 mg., calcium 10.5 mg., phosphorus 5.2 mg., per 100 cc. of blood. His gastric analysis showed 64 units of free hydrochloric acid forty-five minutes after the start of the test. He made an excellent recovery following prompt feeding of a gelatin-milk diet, which was rapidly increased in calories by the addition of cereals and eggs.

Case II. J. LaD., Jr., a son of Case I, was a male child of six and a half years of age who developed his disability at birth. Following the delivery of the patient, it was found that the head of the humerus was separated from the shaft on each side. At one year of age, he fractured his left femur at the neck, when he fell out of his carriage. At twenty months of age, he fell while playing with his sister and fractured his right femur. There was marked callus formation visible on the roentgenogram. The calcium content of the blood was 10.4 mg. and the phosphorus was 4.9 mg. per 100 cc. of blood.

FIG. 8. Case II. Fracture of the femur on the right side and thickening of the left femur at previous fracture site are shown.

FIG. 9. Case II. Fracture of the femur with overriding. The flask-shaped dilatation of the lower end of the femur and the fine trabeculation are also shown.

Subsequently, he fractured his femurs several times in different areas. These did not always heal properly and left overriding and bowing. There was exuberant callus present. Once while in bed for the healing of one fracture of the femur, he turned suddenly and fractured the femur of the opposite side. At the present time, this patient is under the care of a convalescent orthopedic hospital.

SUMMARY AND CONCLUSION

Two cases of osteogenesis imperfecta of the tarda type are described. The "tarda" type is also called fragilitas ossium by some authors. The literature bearing on the etiology, pathogenesis, histopathology, and treatment has been reviewed.

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ROENTGEN ANATOMY OF OBLIQUE VIEWS OF THE LUMBAR SPINE

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FREQUENTLY in consultations we have had difficulty in making ourselves clear with reference to the roentgen anatomy of the lumbar spine. The anatomy of this section of the skeleton is admittedly complex when studied in three-dimensional plane, and is even more confusing when all planes are seen as one on the roentgenogram, especially when oblique views are being examined. Some have dismissed this subject as requiring no explanation for the experienced, difficulty being met with only by the novice. However, we have often been in the position of finding it hard to answer questions put to us about roentgen anatomy and for this reason the present detailed study of oblique views of the lumbar spine was made.

We undertook to roentgenograph the dried disarticulated skeleton in the oblique positions commonly used, and to correlate the findings on the roentgenograms with the actual specimen. In this way it was possible to identify on the roentgenograms all the anatomical features in the dried vertebrae. In order to prove beyond question which apophyseal joints we were looking at we placed the lead letters "R" and "L" on the respective sides attached to the transverse processes. Then we outlined with ink the anatomical features clearly seen on the roentgenograms (Fig. 1 and 2). The lumbar and lumbosacral apophyseal joints usually lie in most subjects at an angle of about 45 degrees with coronal plane of the body slanting toward the midline from posterior to anterior. The superior articular processes lie lateral and anterior to the inferior articular processes. Next, roentgenograms were made in both anterior and posterior oblique positions of the lumbar spine of the living subject. Then direct comparisons revealed the features shown in Figure 3.

In our experience most difficulty seems to arise in deciding which side structures one is viewing on a given oblique projection. It is, of course, essential that the roentgenologist know exactly how his technician positioned the patient. Reference to the drawings in Figures 4 and 5 will help to make the anatomical situation

TABLE I

Table Aspect	Tube Aspect	Apophyseal Joints Visualized
1. With patient semi-supine Position		
Right posterior oblique	Left anterior oblique	Right
Left posterior oblique	Right anterior oblique	Left
2. With patient semi-prone Position		
Right anterior oblique	Left posterior oblique	Left
Left anterior oblique	Right posterior oblique	Right

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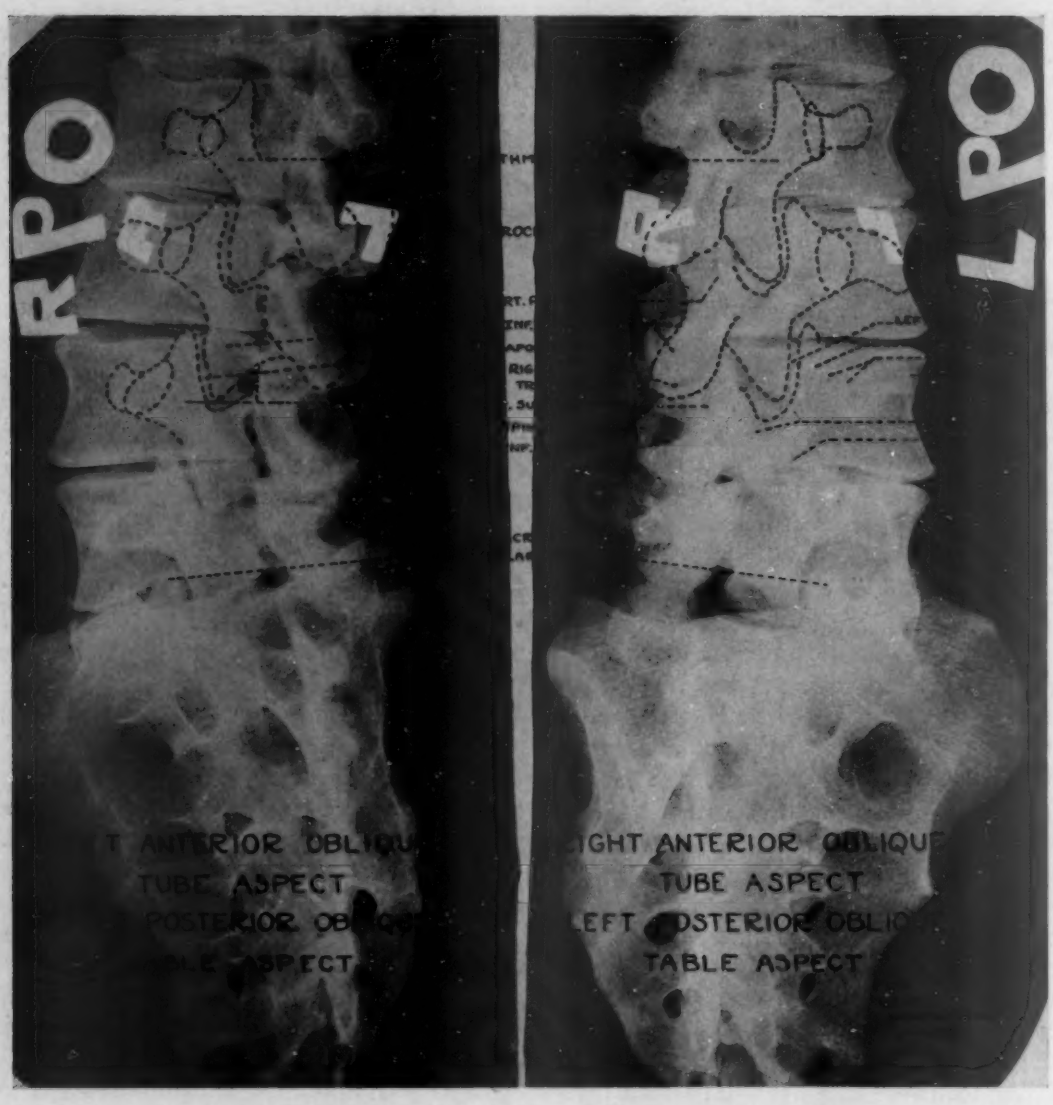

Fig. 1. Outlined features in roentgenograms of disarticulated lumbar spine taken in the right and left oblique position indicated. These were taken in the posterior oblique position with reference to the table (RPO-LPO), a position commonly recommended in books on technique. In this case the apophyseal joints of the side next to the table are shown. If one considers these as anterior positions with reference to the tube (LAO-RAO), then opposite joints to the side nearest the tube are shown.

more clear. One sees in these opposite positions just how the apophyseal joints are brought into line by anterior or posterior rotation of the patient approximately 45 degrees. When a subject lies, let us say, on the right side of his back and then on the right side of his abdomen, apophyseal joints of opposite sides are visualized. Some name the positions with reference to the tube; others refer to the table. All this has caused considerable confusion. However, in our studies it was found that regardless which position was used or which method of terminology was applied, all posterior oblique views showed the apophyseal joints of the same side and, vice versa, all anterior oblique views showed the opposite joints. For example, a right posterior oblique view

FIG. 2. Features outlined with ink in roentgenograms of dried lumbar spine taken in the anterior oblique position with reference to the table top (RAO-LAO). It will be noted that if one considers these anterior positions then opposite apophyseal joints to the side next to the table are shown. If one considers them posterior with reference to the tube (LPO-RPO), then the joints of the side next to the tube are shown.

and a left anterior oblique view both showed the right apophyseal joints.

Most papers that have been written on this subject show the patient in an anterior oblique position with reference to the roentgen tube; that is, with the side to be roentgenographed next to the film. Much is to be said for the position and we use it routinely. However, in certain cases or for check comparison for particular joints, the posterior oblique position may be useful. In their recent book on technique Files[2] and his associates show only this position for oblique views of the lumbar spine.

In the right anterior oblique position (Fig. 4) the patient is shown lying semi-supine on a table with the transverse axis of the body rotated toward the tube at an angle of 45 degrees with the table top. This degree of angulation we have found satis-

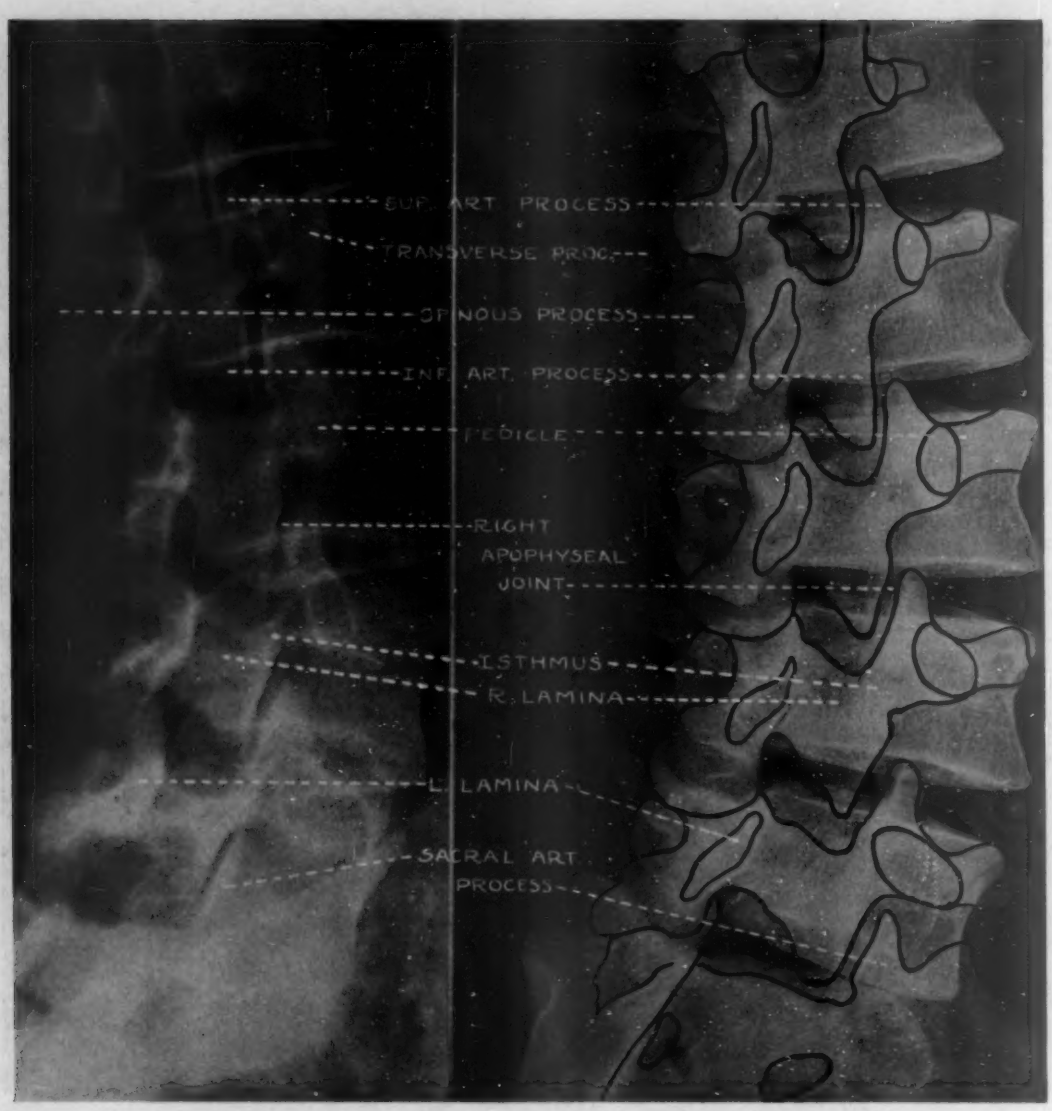

Fig. 3. Here shown are the roentgenograms of the living spine at the left and of the dried spine at the right both taken in the right posterior oblique position with reference to the tube as indicated in Figure 5.

factory in the great majority of cases to show the lamina, isthmus (pars interarticularis) and zygapophyseal joints on the side desired (Fig. 1). In any given case, however, it may be necessary to vary the angle from 35 to 45 degrees. An increase is rarely required because the articular facets tend to turn towards the sagittal rather than the coronal plane when variations do occur. Ghormley and Kirklin[3] recommended 32 degrees as the optimum angle for visualization of the posterior articulations at the lumbosacral joint. The accompanying drawing (Fig. 4) shows the manner in which the central ray is directed parallel to the surface of the obliquely placed left articular facets when the body is rotated forward at the proper angle, and how the opposite side facets are obscured by not being parallel to the central ray. Comparison of the roentgenograms of the living spine and the outlined dried specimen shows clearly the

anatomical features to be seen (Fig. 3).

In the right posterior oblique position shown in Figure 5 the patient is seen facing the table with the side to be roentgenographed rotated towards the tube with the transverse plane of the body at an angle of 45 degrees with the table top. Here, by referring to the drawing, it is seen that the right articular facet is visualized because its axis lies parallel to the central ray while the left articular facet is obscured because its axis is at a right angle to the central ray. The anterior oblique position affords a shorter object-film distance of the lamina and the apophyseal joints as compared with the posterior oblique position and should therefore show less distortion, but actually this factor seems negligible. It may at times be desirable to get two views of the same parts to show a slightly different aspect, and these two positions may then be compared for variation. Needless to say, simple reversal of positions shown will delineate the opposite side structures of the vertebrae, so that if one wishes two views of the left apophyseal joints, lamina and isthmus, he could take right anterior oblique and left posterior oblique views to show them (see Table 1).

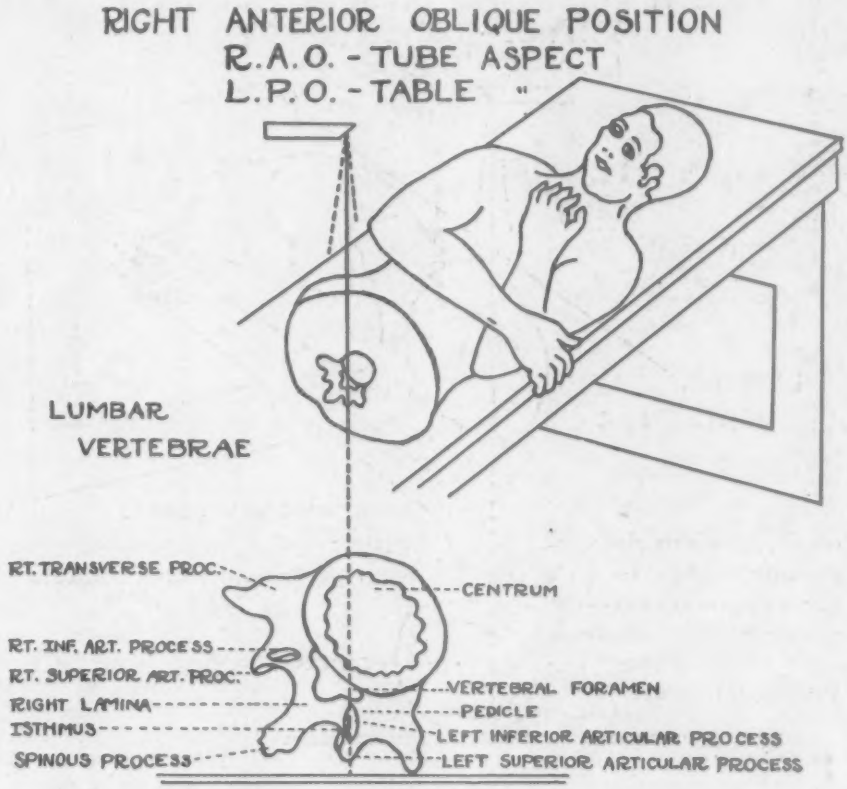

Fig. 4. Showing mechanism for visualization of the left apophyseal joints by approximately 45 degrees anterior rotation. Note decreased object-film distance.

When oblique views are made of the lower lumbar or lumbosacral region, it will be observed that the sacroiliac joint of the side opposite the visualized apophyseal joints will be clearly brought into view. This is because the axes of the sacroiliac joints are opposite to those of the apophyseal joints. They slant forward but laterally forming an angle of about 45 degrees with the coronal plane while, as has been shown above, the apophyseal joints slant in an

opposite direction; namely, forward and medially. Thus, when the right apophyseal joints are visualized, the left sacroiliac joint is seen, and vice versa, regardless of whether the position is anterior or posterior or with reference to table or tube.

In everyday practice one frequently rotates a patient in the position shown in Figure 5 in order to throw the gallbladder away from the spine. In such cases it is often noticed how clearly the posterior articulations are shown, and from the above consideration it will be seen that these are the right side joints. Similarly, routine views of the stomach are made with the patient in the left posterior oblique position and the left apophyseal joints are clearly delineated in these roentgenograms.

From the above it will be appreciated that adequate visualization of the posterior articulations, isthmus and lamina is possible only by use of oblique views in study of the lumbar spine. Once the roentgen anatomy is thoroughly understood and is clear, as we believe this method of study makes it, interpretation is much easier. It will be seen that the superior and inferior articular processes and facets are clearly shown, as well as the joints between them (the zygapophyseal, apophyseal, or posterior articulations as they are variously called), the pars interarticularis or isthmus, the lamina and spinous processes, pedicles, and transverse processes (Fig. 3). Which side these structures are on can readily be determined by marking the films RPO, LAO, etc., with reference to the side nearest the tube or, if one wishes, marked with

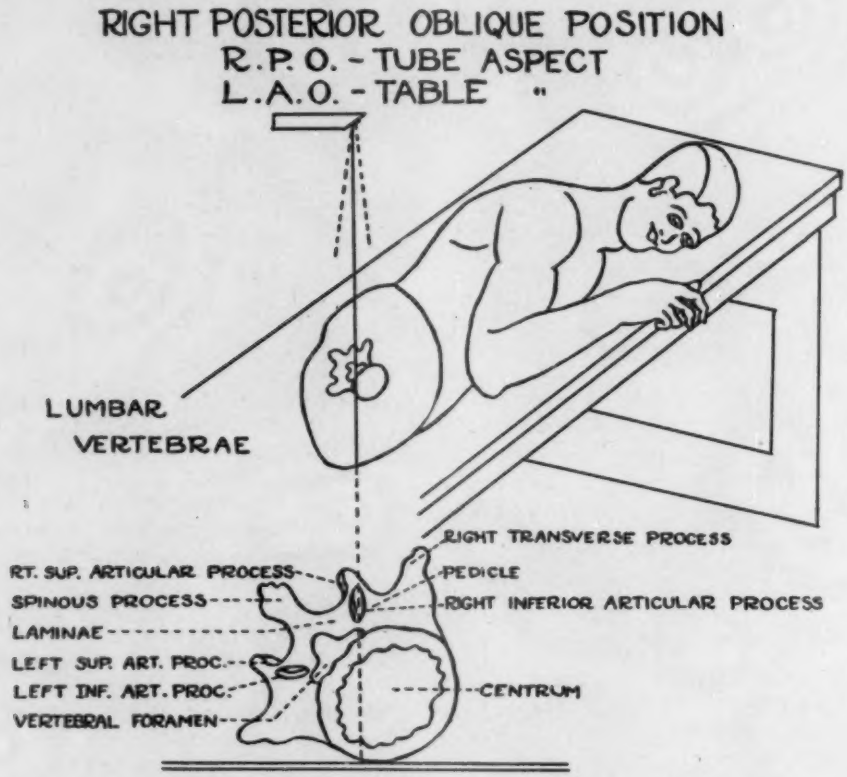

Fig. 5. Showing mechanism for visualization of the right apophyseal joints by approximately 45 degrees posterior rotation. Note increased object-film distance.

reference to the table, it being only necessary to have it understood by the technician which way the roentgenologist prefers it.

A number of papers[4,6,10] have appeared in the roentgen literature detailing the pathological conditions of the lumbar spine which can best be delineated by oblique views, and these are: fractures of facets, isthmus, pedicle, lamina; erosions and bone destruction from tumors; developmental anomalies of the spinous process, lamina or isthmus; dislocation or subluxation, and arthritic changes such as narrowing, spurs, irregularities, and so forth.

It has seemed to us in studying the literature on the subject that many excellent papers have assumed a complete knowledge of the roentgen anatomy of the lumbar spine, particularly of oblique views, and have not made it perfectly clear to readers what parts are being visualized and why. Moreover, little or nothing has been written about the posterior versus the anterior oblique views and it is desirable to understand the difference with reference to which parts are visualized in the two positions. We hope the method of study outlined here may help to clarify the subject for others as it has for us.

Most of the work on this paper was done while the authors were associated in the X-Ray Department of the 115th General Hospital in Yorkshire, England, 1944–1945. We wish to acknowledge with thanks our indebtedness to Dr. C. Guy Hitchcock, Radiologist at the General Hospital, Harrogate, Yorkshire, England, for his loan of the lumbar spine used in this study.

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ROENTGENOLOGIC RECOGNITION OF RADIOPAQUE SPONGES*

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INTRODUCTION

SURGICAL sponges and laparotomy pads are the most common foreign bodies accidentally left in the abdominal cavity at operation. Crossen and Crossen[1] collected from the literature a series of 307 cases in which this unfortunate event had occurred. The serious consequences of such an accident are well borne out by the fact that in one-fourth of these patients death occurred.

In spite of preventive measures, such as counting of sponges, stick sponges, and the continuous sponge, this misfortune may happen to the best and most careful surgeon and seems to be unavoidable. Since it appears difficult to completely eliminate the occurrence of such accidents, many efforts have been made to render sponges and laparotomy pads radiopaque. This would permit their detection at any time during or following operation by roentgen examination.

Such efforts would be of little value if all those potentially concerned with the detection of these foreign bodies were not fully aware of their roentgenographic appearance at various time intervals after inclusion in the abdomen. Many physicians are hardly acquainted with the roentgen image cast by radiopaque sponges and laparotomy pads. Also, the literature concerning this problem is rather limited and most current textbooks of surgery and radiology are devoid of this subject. For these reasons, it is believed worth while to report 3 cases in which radiopaque sponges and gauze pads were detected in the abdominal cavity many months after operation, and to discuss briefly certain aspects of the roentgenographic appearance and diagnosis of these foreign bodies.

CASE REPORTS

CASE 1. This female patient was admitted complaining of dysuria and lower abdominal pain of nine days' duration. Three months prior to admission the patient had undergone a uterine suspension in another hospital. The physical examination was not remarkable except for excoriation of the vulva due to urinary incontinence. The laboratory examination disclosed albuminuria, hematuria, and pyuria. *B. proteus* was cultured from the urine.

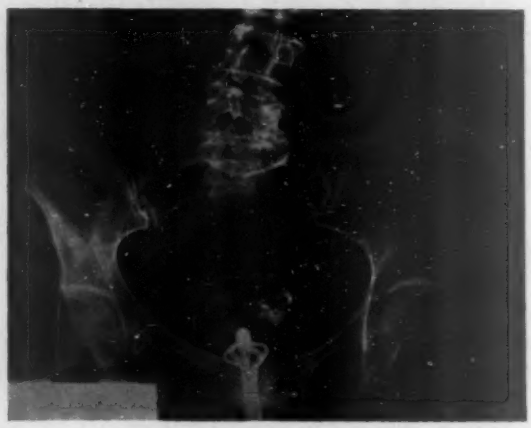

FIG. 1. Case 1. Coiled strings in bladder area represent the radiopaque insert of a sponge. This type of sponge is also shown in Figure 4*B*.

Intravenous pyelographic studies disclosed bilateral hydronephrosis and opaque material having the configuration of coiled strings in the bladder area (Fig. 1). On subsequent cystoscopy, edema and inflammatory changes of the mucosa with multiple punctate hemorrhages were seen. A black foreign body surrounded by soft white encrustations was noted adherent to the left wall of the bladder. Because of these findings, a suprapubic cystotomy was performed, and a gauze sponge containing a radiopaque insert was removed from a contracted bladder. The patient made an uneventful recovery.

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Case II. This female patient was admitted complaining of intermittent periumbilical pain associated with nausea, anorexia, constipation, and considerable weight loss in two months. Nineteen months before, a hysterectomy and bilateral oophorectomy had been performed at another hospital. The patient was apparently well until seven months prior to admission when she began having episodes of abdominal pain lasting about one week at a time. For the last two months the pain had become almost constant and a mass had appeared below the region of the umbilicus.

Physical examination disclosed a tender, fixed mass about 7–8 cm. in diameter in the lower mid-abdomen. The patient had an elevated temperature. The laboratory data revealed moderate secondary anemia and leukocytosis.

Roentgenologic examination of the colon by barium enema showed a large mass in the mid-abdomen which contained numerous small gas shadows and an irregular mottled opaque density in the center (Fig. 2). The large and small intestine were displaced by this mass towards the flanks and epigastrium. On the basis of these findings a diagnosis of a retained laparotomy pad or sponge was made. On operation, a gauze pad was removed from a large abscess cavity formed by matted intestinal loops. The patient subsequently recovered.

Case III. This female patient was admitted eight months following a hysterectomy at another hospital. She complained of 80 pounds weight loss, marked weakness, anorexia, nausea, and vomiting.

The physical examination revealed a marked cachexia. A questionable mass could be felt anterior to the cervix on pelvic examination. The laboratory examinations disclosed a marked hyperchromic anemia, the etiology of which could not be determined at the time of admission. There was also a low grade fever and elevated sedimentation rate.

The roentgenologic examination of the large intestine by barium enema did not disclose any intrinsic pathologic changes. On subsequent film studies of the abdomen, a pelvic mass was recognized containing mottled gas shadows. Within this mass was noted an irregular opaque shadow consisting of small granular densities (Fig. 3*A*). Because of these findings, the presence of an opaque gauze pad was suspected, and a laparotomy was performed. The operation disclosed the presence of a laparotomy pad in the pelvic peritoneal cavity which had perforated into the ileum. The patient subsequently made an uneventful recovery.

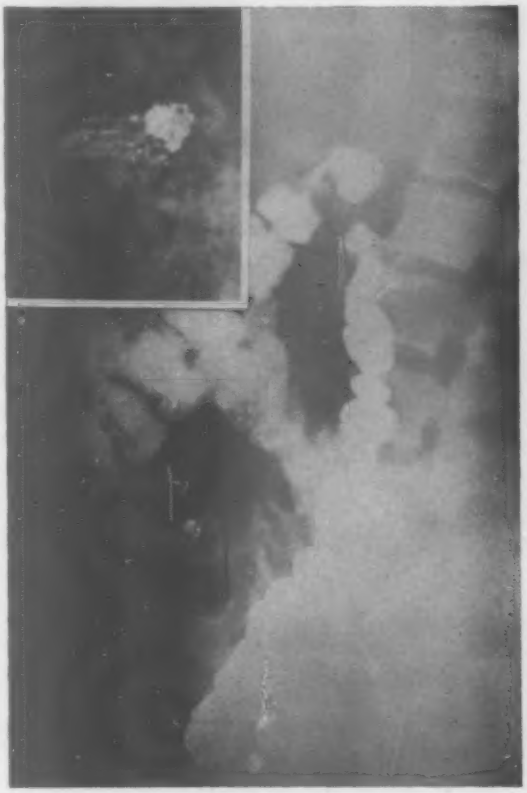

Fig. 2. Case II. Lateral view of abdomen following barium enema. The granular opaque insert of the laparotomy pad is clearly visible. This type of insert is shown in Figure 4*D*.

DISCUSSION

Cotton gauze imbedded in the body does not cast a shadow on roentgenologic examination. For this reason many attempts have been made to render objects made of gauze radiopaque. Earlier workers accomplished this by attaching metal rings or metal markers to sponges and lap packs.[2,3] The introduction of contrast gauze constituted definite progress in this field. This material consisted of gauze into which metal wires, or threads impregnated with radiopaque substances, were woven. The somewhat expensive and tedious manufacture of contrast gauze, as well as certain

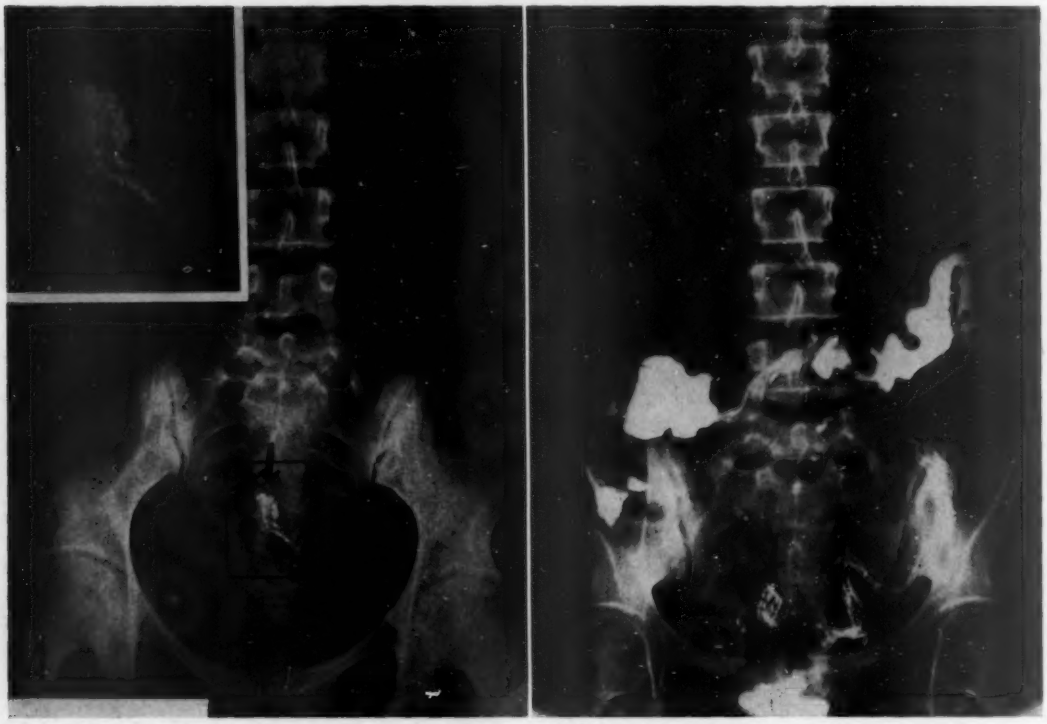

Fig. 3. Case III. *A*, roentgenogram of abdomen disclosing radiopaque insert of laparotomy pad. This type of insert is represented in Figure 4*D*. *B*, roentgenogram following evacuation of barium enema. Note that radiopaque insert closely simulates the pattern of intestinal mucosa.

Fig. 4. Roentgenogram showing various types of radiopaque inserts included in sponges and laparotomy pads. See text.

undesirable physical properties precluded its widespread use. Recently, Lewison[4] investigated experimentally a number of radiopaque substances with regard to roentgenographic characteristics and tissue reaction. His findings prompted him to advocate the insertion of pliable lead glass fibers into surgical sponges and laparotomy pads.

Radiopaque sponges commercially available* contain barium sulfate as contrast medium in a suitable binding material. Carbon is included in the radiopaque insert so that it may be easily recognized on direct inspection. The two types of sponges available in this country are shown with their corresponding roentgenograms in Figure 4. It will be noted that in sponges of one type (Fig. 4*A*) the radiopaque medium is cast into a long string. An older modification of this sponge utilized cotton thread impregnated with contrast medium (Fig. 4*B*). This type of sponge was recovered from Case I. The second type of sponge contains between its layers a gauze insert to which the opaque mass has been firmly applied. In older modifications of these inserts the opaque medium appeared somewhat unevenly distributed (Fig. 4*D*, Cases II and III), but recent types demonstrate uniform and heavy distribution of the contrast medium throughout the meshwork of the insert (Fig. 4*C*).

It should be emphasized that the roentgenographic image of the opaque insert may vary greatly with the position and folding of the sponge. This will be appreciated in the roentgenograms of the sponges (Fig. 4), as well as the roentgenograms of the cases described above. In addition, the examiner should realize that diffusion and penetration of the contrast medium into the meshwork of the insert or surrounding gauze may occur. Once the sponge has remained for some time in the body, the opaque mass may have a somewhat granular and mottled appearance (Fig. 2 and 3). Though this may hardly affect the opacity of the foreign body, it contributes nevertheless to a definite change of the roentgenographic pattern of the insert. This is demonstrated to advantage by comparing the roentgenogram of a new insert with one which had remained in the abdomen for eight months (Fig. 5).

The radiopaque mass may to a certain extent resemble the mucosal folds of the

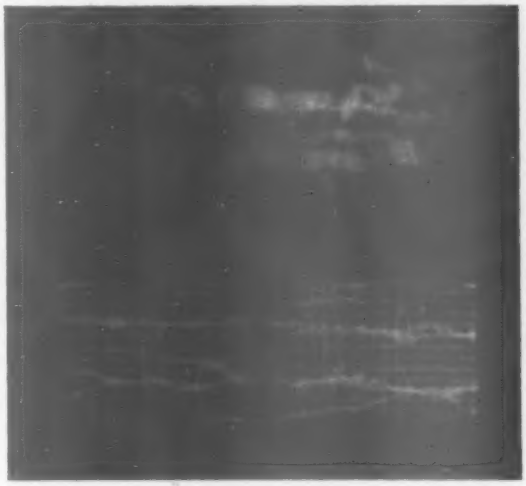

Fig. 5. Case III. Changes in roentgenographic pattern of insert which had remained in abdomen for eight months. Comparison with fresh insert.

intestinal tract. In a roentgenogram following evacuation of a barium enema, the opaque sponge appeared so close to the rectum and simulated its mucous membrane to such an extent that its presence could hardly be appreciated without the aid of a survey roentgenogram of the abdomen (Fig. 3, *A* and *B*). Two of the patients in whom the presence of a foreign body was not suspected clinically were referred to the Roentgen Department for gastrointestinal studies. In these patients there was a distinct danger of overlooking the opaque insert on roentgenoscopic screening and roentgenograms following administration of contrast medium.

The variety of radiopaque sponges available interferes perhaps to some extent with their proper recognition. It is felt that a standardization of the radiopaque inserts,

*We are indebted to the Bauer and Black division of the Kendall Company, and to the Johnson and Johnson Company, for supplying us with information concerning radiopaque sponges commercially available.

as well as publication of their roentgenographic image in medical journals and textbooks of surgery and roentgenology, would certainly contribute to easier identification of these foreign bodies.

SUMMARY

1. Three cases are described in which radiopaque sponges and laparotomy pads were detected on roentgen examination three, nineteen, and eight months following abdominal operations.

2. Various types of radiopaque sponges commercially available are described and illustrated by roentgenograms.

3. Certain factors which cause a change of the roentgenographic pattern of these foreign bodies are briefly discussed and difficulties in their roentgenologic detection are pointed out.

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Vol. 61, No. 5

STERILE PYURIA*

By KILE C. HARDESTY, M.D.
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TWO cases of an unusual type of urinary disorder, which can be diagnosed readily by the roentgenologist, have been seen at this hospital. The chief manifestations are those of an acute cystitis with marked thickening and edema of the bladder wall which reduces its capacity to a few cubic centimeters. This swelling compresses the intramural portion of the ureters to such an extent that the urinary back pressure causes a varying degree of ureterectasis and caliectasis. The urine contains large numbers of pus cells and at times red blood cells but no organisms can be identified as the etiologic agent.

The patient's symptoms are those commonly associated with a severe bladder infection. Ordinary urinary antiseptics have little or no effect in relieving the patient's discomfort or in clearing up the pyuria. The most striking thing about this condition is the dramatic response to intravenous arsenicals. In a very few days a patient who has suffered for a considerable time with burning, frequency and stranguria can be relieved of all these symptoms.

CASE REPORTS

CASE 1. C. M., a white male, aged thirty, was admitted to the hospital December 9, 1945, with a tentative diagnosis of carcinoma of the bladder. His chief complaints were frequency, burning on urination, extreme urgency, and nocturia. He gave the history of having been under the constant care of a urologist for the previous two months during which time he had received penicillin almost continuously and several courses of a sulfa drug with little or no relief from his symptoms.

Physical examination revealed a man of about the stated age who appeared to be in great discomfort. His temperature was 99.6° F. and urine dribbled from the urethra almost continuously. Laboratory studies revealed the hemoglobin to be 73.1 per cent (12.5 gm.), red blood cells 4,070,000, white blood cells 10,950 with 74 per cent neutrophiles and 26 per cent lymphocytes. Kahn and Wassermann tests were both negative. The urine was yellow and cloudy, alkaline in reaction, specific gravity 1.010, albumin one plus and negative for sugar. There were innumerable white and red blood cells mixed with clumps of mucus. Smears of pus from the urine were negative for acid fast bacilli and other organisms. Urine culture showed no growth at the end of seventy-two hours.

Cystoscopic examination was attempted but could not be tolerated by the patient. An intravenous urogram showed a small contracted bladder measuring about 3.5 cm. in diameter when completely filled. The renal calices were moderately dilated bilaterally. The ureters were dilated throughout their entire course except for the intramural portion which was constricted by pressure from the swollen bladder wall. There was a 1 cm. break between the visualized lower ends of the ureters and the dye filled bladder which was interpreted as representing greatly thickened, edematous bladder wall (Fig. 1*A*).

Treatment consisted of urinary sedatives and antispasmodics in addition to two tablets of pyridium four times daily with one grain of codeine hypodermically every four hours to control pain. He was given 50,000 units of penicillin every three hours. At the end of a week on this regimen the patient stated that he thought that there might be some lessening of his symptoms.

On December 16, he was given 0.03 gm. of mapharsen intravenously. This was repeated on December 18 at which time he was sure that there had been a definite diminution in the severity of his symptoms. The mapharsen was continued on alternate days until a total of five injections was given. Before this course of therapy was completed he was up and about the ward experiencing very little discomfort. He

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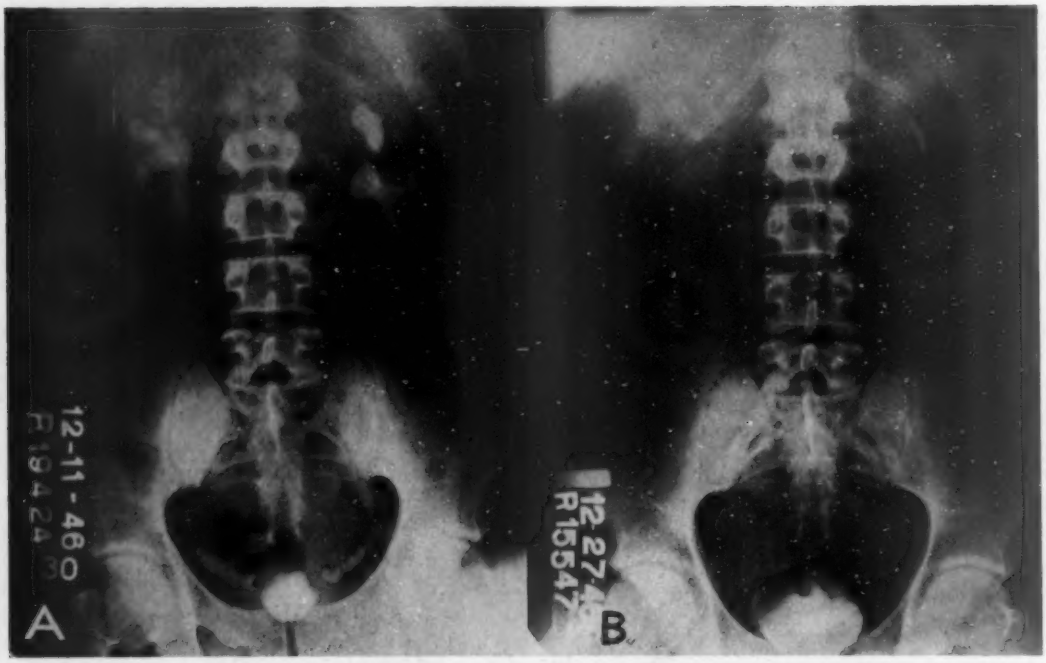

FIG. 1. Case I. *A*, intravenous urogram made during the acute phase, showing markedly contracted bladder, with dilatation of ureters and calices. The intramural portions of the ureters are not visualized and the space indicates the thickness of the bladder wall. *B*, urogram after recovery is nearly complete, showing normal ureters, pelves and calices.

could go two hours without voiding and then had only infrequent attacks of burning and pain.

A urogram done on December 27 showed the ureters and kidneys to have returned to normal. The bladder at this time measured 7.5 cm. in diameter and appeared fairly normal (Fig. 1*B*).

A cystoscopic examination was done January 7, 1947, with very little discomfort to the patient. The entire bladder wall was slightly edematous. Some of the vessels were more prominent than usual and engorged. Both ureteral orifices were edematous, white in color and a little patulous. There was no residual urine in the bladder.

He was discharged on January 15 with no burning, frequency or nocturia. The urine was entirely negative.

CASE II. G. R., a white male, aged thirty, entered the hospital because of frequent, painful urination. He stated that on the morning of November 12, 1946, he awoke and noticed that the sheet was spotted with a mucoid material which might have been urethral discharge or urine. He denied any extramarital exposure. He developed pain on urination which was present only during the act of micturition. He went to his family doctor who made a smear which was negative for gonococci. The doctor gave him pills which turned the urine blue but the frequency and nocturia developed to such an extent that he was voiding every ten minutes and felt as though he were passing steam. He was placed in a hospital and given penicillin and a sulfa drug for seven days. His symptoms did not improve and he started passing small blood clots, so he was referred to a urologist.

The urologist made repeated smears and cultures, all of which were negative for tubercle bacilli or pyogenic organisms. The prostate was found to be normal. At no time did he have chills or fever. After a month of steady treatment, during which he showed no improvement, he was referred to this hospital.

A routine examination showed 5,500,000 red blood cells per cu. mm. with 16.2 gm. hemoglobin. The white blood count was 12,800 with segmented cells 65 per cent, juveniles 4 per cent,

lymphocytes 22 per cent, monocytes 4 per cent, eosinophiles 4 per cent, and basophiles 1 per cent. The Kahn and Wassermann reactions were both negative. The urine was cloudy and contained a three plus bile. The reaction was acid, specific gravity 1.011, albumin two plus, sugar negative, and many white blood cells were seen. Smears and cultures were negative for organisms.

An intravenous urogram done on January 22, 1947 showed a contracted irregular bladder with a thickened edematous wall. The terminal ureters showed a bulbous dilatation. The kidney pelves and calices were normal (Fig. 2*A*).

Intravenous mapharsen 0.03 gm. was started January 23 and given every second day for three doses. The amount was then increased to 0.06 gm. and continued at the same interval until five additional injections were given. The patient's symptoms improved steadily. A urogram on February 6 showed a marked increase in bladder capacity but the walls were still thickened and the ureters moderately dilated (Fig. 2*B*). A cystogram done the following day revealed a bladder of normal size. At this time the patient could go six hours without voiding and the urine was free of pus.

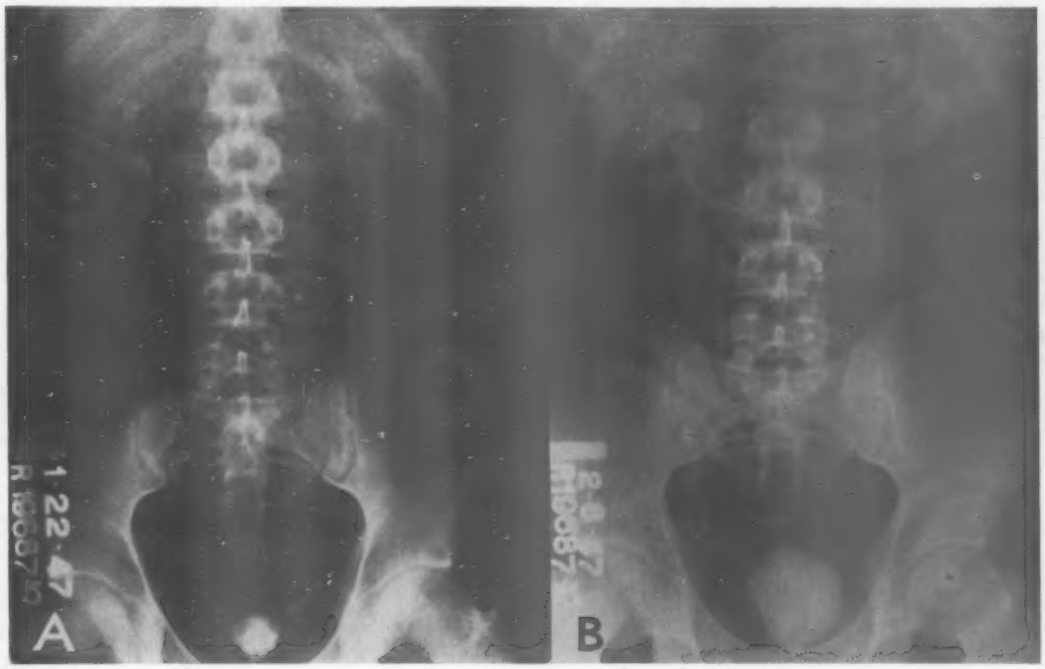

Fig. 2. Case 11. *A*, urogram made during acute phase, showing contracted bladder with bulbous dilatation of lower ureters. Note irregular bladder outline and thickness of the wall. *B*, urogram taken during early recovery showing increased capacity of the bladder and decrease in the thickness of its wall. There is still some compression of the intramural portion of the ureters which causes a small amount of dilatation above.

DISCUSSION

This condition has been given various names by different observers, such as amicrobic pyuria, abacterial pyuria and acute interstitial cystitis. Tissue examination has revealed areas of lymphocytic infiltration together with areas of hemorrhage. The most common finding was distended capillaries filled with red blood cells. This was so marked in one case that the pathologist suggested the possibility of hemangioma of the bladder wall.

The etiologic agent is yet to be discovered. Since stained urinary sediment and cultures as well as guinea pig inoculation all fail to demonstrate an organism

associated with this disorder, speculation leads one to consider a spirochete or filterable virus.

The importance of recognizing this condition early is understood when one notes that the diagnosis of carcinoma of the bladder is sometimes made and as the result patients may come to needless surgery. In one reported case this was prevented by the roentgenologist, who recognized the condition and insisted that the urologist restudy the case before doing a cystectomy. Also correct diagnosis will insure the patient of proper treatment before irreversible changes occur in the bladder, ureters or kidneys.

SUMMARY

Two cases of a urinary disorder, having the symptoms of a severe cystitis without demonstrable organisms in a urine containing large numbers of pus cells, are presented. The characteristic roentgen findings which consist of a greatly contracted bladder with a thick edematous wall compressing the intramural portion of the ureters causing a secondary dilatation of the upper urinary tract are illustrated.

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The encouragement and help given by Dr. Charles L. Martin in the preparation of this manuscript are gratefully acknowledged.

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DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

A SIMPLE, INEXPENSIVE SET OF PRISMS FOR VIEWING STEREOSCOPIC ROENTGENOGRAMS

By CHARLES C. GASS, M.D., *and* CAPRES S. HATCHETT, M.D.
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OMAHA, NEBRASKA

SOME radiologists are able to voluntarily cross their eyes, dissociate accommodation, and obtain a stereoscopic image from two stereoscopic roentgenograms placed before them on a viewbox. A few years ago one of the authors was acting as radiologist in the armed forces in the South Pacific where no stereoscopic viewing device was available. As he was unable to voluntarily obtain stereoscopic fusion, he devised a pair of glasses using prisms to enable him to obtain a steresocopic effect. We have further studied the device during the past year and find it can be constructed for less than ten dollars, can be carried in a vest pocket, and can be used anywhere to study stereoscopic roentgenograms. We have found no one unable to get a three dimensional image with this device regardless of previous experience with stereoscopy.

There is no similar device described in the roentgenographic literature that we have been able to discover. In 1930, Hadley[2] described a stereoscopic viewing device using 90 degree silvered prisms which were rotated around their vertical axes to give stereoscopic fusion of films viewed side by side on a viewbox. Caldwell,[1] in 1918, described a somewhat similar device using plain 90 degree prisms which were rotated around their vertical axes and were also adjustable for interpupillary distance. In 1929–1930 there were several references in the French literature to hand devices made by Benoit and others.[3] These were constructed somewhat like an opera glass with various prisms, lenses and diaphrams.

Our device (Fig. 1 and 2) consists of two prisms set in frames, used for spectacles, with the thick ends of the prisms directed laterally. These can be obtained from any

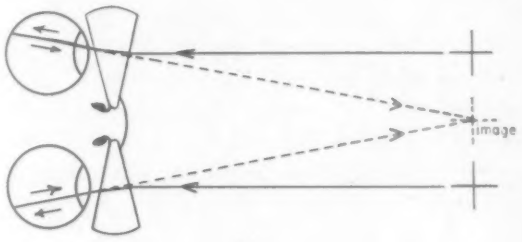

Fig. 1

Fig. 2

optical company at a cost of from six to seven dollars. The prisms may be of any strength from about 9 to 20 degrees. The greater the strength of the prism, the shorter the distance at which the films may be viewed. A set of 11 degree prisms fuses the stereoscopic films at about 130 cm.

(52 inches). The 20 degree prisms allow visualization at about 60 cm. (24 inches). The two films are placed side by side on a viewbox and are examined by looking directly at them. The eyes should be relaxed as for distant vision. At first it may be necessary to move the head slightly back and forth to vary the distance from the films to get good fusion. After a few trials, fusion is immediate. Three images are seen; the middle image is the most distinct and is seen in three dimensions. Careful, detailed examination may be done without loss of the stereoscopic effect. The prismatic glasses may be used over regular glasses if desired. A lorgnette frame might be desirable in some cases. There is no correction necessary for different interpupillary distances. We have used the same glasses for persons with interpupillary distances ranging from 65 to 75 mm. All size films may be viewed from the smallest to the 14 by 17 inch. We have used them to view stereoscopic 4 by 5 inch photoroentgen chest films.

The normal stereoscopic image may be obtained with the eyes viewing the part from the same position as the tube, or the reverse image may be obtained with the part viewed from the opposite side. There is some difference from the conventional stereoscope in that to obtain the normal image it is necessary to place the film conventionally seen by the left eye on the right side of the two side by side films. Putting it on the left gives the reverse stereoscopic effect.

The only respect in which we have found the images less satisfactory than those of the conventional stereoscope is that there is slight chromatic aberration of structures lying along the vertical axis in respect to the prisms. This is more pronounced with prisms of greater strength, but has not been marked enough to cause us any difficulty. If this is found individually undesirable, achromatic prisms may be used.

We believe the most practical prism to be 20 degrees. This gives close enough vision to easily study details. Higher strength prisms give greater chromatic aberration. They also cause slightly greater difficulty of fusion.

SUMMARY

We believe the device described above to be a practical prism stereoscope. It can be carried on the person at all times without difficulty. It can be used in small offices where conventional stereoscopes are not available. Roentgenograms may be viewed at any time at home, at the patient's bedside, or even outside using sunlight. It will apparently be satisfactory for all normal eyes regardless of interpupillary distance and regardless of previous proficiency at stereoscopy. So far as we can discover, the device has not been previously described in the roentgenographic literature, although we feel sure it has been used because of its simplicity.

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EDITORIALS

RADIATION HYGIENE

THE making of the atom bomb was complicated by the most extraordinary health hazard that the world has ever known, insidious in the extreme, inappreciable to the senses, late to reveal the injuries produced and only to be detected by methods novel to the usual guardians of health —the physicians. The control of this hazard was the achievement of a unique cooperative effort by physicists, chemists and physicians, and the special scientific discipline developed received the name: Health Physics. On this is founded a special branch of Industrial Preventive Medicine which we can call Radiation Hygiene: the art of avoidance of injury by radiating machines and radioactive products.

A special feature of military preparedness which might be called Radiation Damage Control will require a careful assessment of the tolerance of personnel to radiation. The acceptable peace-time limits might require modification during an emergency with an attendant increase in the risk of injury by radiation—the exigencies of warfare often requiring levels high enough to permit manifest damage yet avoiding unnecessary loss of life. As we consider this prospect, we call to our statesmen to mobilize all their powers of persuasion, understanding, conciliation and enduring idealism to prevent a possible need for such measures in the future.

With the availability of radioactive isotopes for medical and industrial researches and ultimate wide application, the need for training in radiation hygiene is spreading to medical schools and hospitals, and to research institutes and factories. Not only the industrial surgeon and the radiologist must take this up, but every physician must learn its fundamentals. Some knowledge of radiation hazards and tolerances, and acquaintance with the instruments for detection and measurement will be expected of doctors. Health is a doctor's career, its preservation is his kingdom, and he may not abdicate a portion of it even though it is strange or difficult.

There exists a National Committee sponsored by the National Bureau of Standards to codify the tolerances and protective measures advisable in the various fields of radiation hazard. The product of its labors is not yet available. The Council on Physical Medicine of the American Medical Association, taking cognizance of the presumptive lag in education of practicing physicians in regard to these new hazards, has published a brief report concerning them. This is reprinted elsewhere in this issue. It is obviously designed to alert doctors who are impatient to apply these newly available tools (radioactive isotopes) in research and therapy for the advancement of medical knowledge and improvement in the care of their patients.

The uptake of the opportunities has been impressively rapid (several hundred projects in about 150 institutions). May the uptake in requisite knowledge be accelerated adequately to keep pace with it.

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Sweigart's, York, Pa.

JEREMIAH FLETCHER LUTZ, M.D.
1872-1948

DR. JEREMIAH FLETCHER LUTZ, of Glen Rock and York, Pennsylvania, was born in Baltimore, Maryland, on November 25, 1872. His preliminary education was obtained in the public schools of Baltimore, in the Baltimore Polytechnic Institute, and in Sadler's Bryant and Stratton Business College of Baltimore. He received his degree of Doctor of Medicine from the College of Physicians and Surgeons of the University of Maryland in April, 1894. His internship was in the Baltimore City Hospitals from 1894–1896.

He practiced radiology variously, and at

times concurrently, at Baltimore, Maryland; Harrisburg, Pennsylvania; and York Pennsylvania. During World War I he was chief of the X-ray Department of United States Army Hospital No. 2 at Fort McHenry, Maryland, from July 19, 1917, to May 31, 1920. He was roentgenologist of Sinai Hospital, Baltimore, from 1921 to 1924, of the Baltimore Eye and Ear Hospital from 1921 to 1926, and of the Kernan Hospital for Crippled Children, Baltimore, from 1921 to 1926. He served as a roentgenologist of York Hospital, York, Pennsylvania from 1930 to 1943.

Dr. Lutz was a member of the York County Medical Society, York Medical Club, Pennsylvania State Medical Society, American Medical Association, Philadelphia Roentgen Ray Society, American Association for the Study of Neoplastic Diseases, and a fellow of the American College of Physicians, of the American Roentgen Ray Society, of the American College of Radiology, and of the Radiological Society of North America.

During World War II he served as Associate Radiologist of Medical Advisory Board No. 4, Pennsylvania, and as Chairman of the Procurement and Assignment Committee for Physicians, of York County, Pennsylvania.

He was a thirty-second degree Mason and a member of the Rotary Club. He was a past president of the York County Medical Society.

His contributions to medical literature included articles on litholapaxy, calcinosis universalis, osteogenesis imperfecta tarda and angioendothelioma of bone.

He is survived by his widow, Mrs. Lotta Heathcote Lutz, of Glen Rock, Pennsylvania, and by four children: Lewin, William, Howland and Beatrice.

Death occurred on September 11, 1948 and was due to cerebral arteriosclerosis.

Lewis C. Pusch, M.D.

ROBERT EARL POUND
1893-1949

ROBERT EARL POUND died on February 6, 1949. His friends who knew him as a serene and genial personality with prodigious capacity for work and for service, had little intimation that for years he had had a hypertension. While sitting with Mrs. Pound awaiting dinner with friends in the Harvard Club, he was taken ill, and was taken to the New York Hospital. Shortly after, he lost consciousness and died of a massive cerebral hemorrhage.

Dr. Pound was born in Nettleton, Mississippi, on June 20, 1893. He did his undergraduate work at the University of Missis-

sippi and was graduated in medicine in 1916 at the University of Virginia. During World War I he served overseas and attained the rank of major. Following a number of years as one of the Cole Collaborators, he opened his own office for the practice of radiology. He was also director of radiology at the Lawrence Hospital in Bronxville, New York. He served as trustee and also recording secretary of the New York Academy of Medicine. Less than two weeks before his death he participated in a medical symposium before the New York County Medical Society.

Dr. Pound is survived by his wife, by a son Donald, aged sixteen, a daughter Judith, aged ten; by his father, Mr. Robert L. Pound, of Tupelo, Mississippi, and by a brother, Mr. Frank C. Pound, also of Tupelo.

Ramsay Spillman, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

American Radium Society
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1949, to be announced.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: Atlantic City, N. J., June 8–10, 1949.

Alabama Radiological Society
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Next meeting time and place of Alabama State Medical Association.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Brooklyn Roentgen Ray Society
Secretary, Dr. Joseph Daversa, 603 Fourth Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. R. Hannan, Cleveland Clinic, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday of October and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Houston X-ray Club
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Louisville Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual Meeting: May 20 and 21, 1949, Bedford Springs Hotel, Bedford, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Ralph E. Alexander, 101 Medical Arts Bldg. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Denver, Colo., August 18, 19, 20, 1949.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. C. J. Nolan, 737 University Club Bldg., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon. 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, February 3 and 4, 1950.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. W. F. Reynolds, University of California Hospital, San Francisco. Meets from January to July, 1949, at Lane Hall, Stanford University Hospital, and from July to December 1949, at San Francisco Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 p.m.
Medical Members' meeting, on third Friday in each month at 5:00 p.m., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 1535 Sherbrooke St., West, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 p.m.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

COUNCIL ON PHYSICAL MEDICINE*

The Council's Consultants on Roentgen Rays and Radium and Medical Aspects of Atomic Energy adopted the following article as one of at least two treatises on atomic energy for publication under the auspices of the Council. The Consultants on Roentgen Rays and Radium and the Medical Aspects of Atomic Energy are: Drs. W. Edward Chamberlain, Arthur C. Christie, Kenneth S. Cole, L. F. Curtiss, Edwin C. Ernst, Gioacchino Failla, Hymer L. Friedell, R. R. Newell, Eugene P. Pendergrass, Ursus V. Portmann, Lauriston S. Taylor, Shields Warren, Stafford Warren and J. L. Weatherwax. The Council appreciates the cooperation of the Consultants on Roentgen Rays and Radium and the Medical Aspects of Atomic Energy.

Howard A. Carter, *Secretary*

RADIATION HYGIENE

Hazards to Physicians, Patients, Nurses and Others from Use of Radioactive Isotopes

W. Edward Chamberlain, M.D.
R. R. Newell, M.D., *Chairman*
Lauriston Taylor, Ph.D.
Harold Wyckoff, Ph.D., *Alternate*
Subcommittee

The atomic age confronts the medical profession with seemingly unlimited opportunities, but equally with the gravest responsibilities. To match the eagerness with which he plunges into investigation of the tremendous possibilities of advance in medical knowledge, the physician investigator must possess the keenest awareness of the hazards to himself, his patients and working associates involved in the study and manipulation of radioactive isotopes and other products of atomic fission. Fundamental is the fact that there is no antidote to radiation injury. Prevention and unrelenting watchfulness are the requirements for what may be called radiation hygiene. Even physicians who are not engaged in this research must have knowledge of the technics involved, for they may have patients who have been exposed to radiations.

The successful technics developed in the Manhattan District and continuously improved and elaborated by the agencies of the Atomic Energy Commission are, of course, available and must be learned. Many of the radiation hazards met in making the atom bomb were quantitatively, and some of them qualitatively, quite different from what the physician will meet as an investigator. The problems of these controls were solved by the work of many men —physicians, chemists, biologists—in cooperation. A new specialist appeared, called "health physicist," who had to devise and apply methods of detection of hazard and of protection against it. With the continual development of new production processes and research technics, the experience and resourcefulness of the health physicists are continually called on. Hygiene remains, however, the obligation of the medical profession, and physicians must not shrug off this department of it merely because they find the health physicists' art difficult to follow and their science difficult to understand.

In using radioisotopes for medical purposes, the physician will usually have access to such consultation. It seems predictable that teamwork will always be necessary. The Atomic Energy Commission delivers isotopes only for use under control of an isotope committee, assuring sufficient breadth of scientific understanding. But even if the physician has a physicist on his team, he cannot leave radiation hazard just to him. He must, himself, take the responsibility for the health of his associates and of his patients.

In the National Laboratories, where radioisotopes are being used, avoidance of radiation has become a way of life. Radioactive materials are transported by special truck in special 200 pound lead pots and put in and taken out under the chaperonage of some one from the health physics department, who constantly measures the gamma ray intensities and keeps a critical eye on the "technic." Similar chaperonage is provided whenever a scientist does a distillation or other manipulation of an important amount of radioactive substance. At regular intervals, twice a week or twice a day, the health physicist goes through the various rooms and passages hunting with a Geiger counter for radioactive contamination on floors and benches, and sampling the atmosphere for radioactive dust. Working in small teams and lacking a "health physicist," doctors are going to have to do these things for themselves. If they are casual about it, as many have been in the handling of radium

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the result will be disaster for all concerned.

Radiation hazard can be put into several classes:

A. External irradiation, beta rays and gamma rays (also roentgen rays)
   1. Injury to patient
   2. Injury to physician and others
   3. Injury to casual personnel
   4. Contamination of laboratories interfering with measurements
   5. Fogging of photographic materials (4 and 5 do not, of course, concern hygiene)

B. Internal irradiation, alpha, beta and gamma
   1. Overdosage, general
   2. Bad distribution leading to local overdose
   3. Pick-up of isotopes by physician and others (*a*) Inhalation, (*b*) ingestion, (*c*) absorption through unbroken skin and (*d*) through cuts or abrasions
   4. Escape of radioactive materials from control with later pick-up by men, animals or plants

External irradiation from isotopes will seldom endanger the patient, who is usually only briefly exposed; the danger is to the doctor and his associates, who are working with these things all the time. The patients' hazards will arise mostly from errors of judgment or blunders in technic: Doctors make errors in dosage of drugs, too, and sometimes need to administer the antidote. Here it must be repeated that there is no antidote to radiation injury.

With isotopes, doctors are using a novel set of units. A millicurie means 37,000,000 disintegrations per second, an amount in milligrams running from about 16 for plutonium to a millionth for radiosodium. The biologic significance of a millicurie varies with the type and energy of the disintegration and the distribution of the isotope in or on the body. It is at least possible that some doctors will make the superficial but erroneous assumption that they know what a millicurie is because they have used millicurie radon implants.

The great hope for the future of isotopes in therapy is the ability of some of them to concentrate in an organ or tissue. This is at the same time a great hazard, for precise dosage depends on precise estimate of how large a volume of tissue will be holding the dose given, when it has become thus concentrated. The effect depends not on the total dose, but on its specific concentration in the susceptible organ. In fact, for alpha emitters and soft beta emitters, account must be taken of uneven distribution within the organ or within the cell, and one must think of dose in disintegrations per cubic micron.

The millicurie is a disintegration rate, and so the biologic dose depends on how long the irradiation lasts. The millicurie dose falls away according to the half-life of the isotope and also by excretory losses from the body. In all these things there is much room for errors in calculation and in judgment, even gross blunders.

Radium, plutonium and radiostrontium are carcinogenic, having long physical half-lives and lie locked up in the bones with very slow excretion. Two microcuries of radium (being radium, this is 2 micrograms), can kill in seven years, a quantity which for many other elements would rightly be considered a harmless tracer dose.

Gamma rays from isotopes in use and in storage physicians already know how to avoid, for they have years of experience with radium. (It is true that many doctors have destroyed their fingers by careless handling of radium.) But the fact of familiarity with radium would tend to make physicians careless with the other things for all have learned to take 50 mg. of radium rather casually. But they have not been giving injections or determining test tube reactions with radium. With radium, one fears lest one lose it. With radioisotopes, one ought to fear lest one spill it. One leaves gamma rays behind when one quits the room. When a beta ray emitter is spilled on the fingers the operator carries with him what he cannot wash off. Moreover, beta rays, being highly absorbable, are biologically extremely effective. So even a small millicurie amount gives a large dose by the time the contaminated cuticle has worn away.

In the chemical laboratory dirty glassware is washed and used again, and spent chemicals are dumped down the drain. Dead animals are carried to the dump or incinerator. Urine and feces go down the sewer. In the isotope laboratory, however, all these may be radioactive. It is a heavy responsibility to see that nothing "hot" is reused and that no dangerous quantities of radioactivity find their way into the sewer, or to an open incinerator or dump. Algae especially, but also higher plants, are capable of reconcentrating some elements which have been diluted and spread on the fields, so that mere dilution cannot be depended on for safety. Wet and dry radioactive wastes have to be collected and isolated, maybe by deep burial.

Many physicians are avid to put radioisotopes to work for medicine, to proceed as fast as

Hazard from Radioactive Isotopes

	Alpha	Beta	Gamma
Proximity Total Body		Doctor, chemist E.g., P, I, Na, Au	Everybody E.g., Ra, I, Co, Na, As, Au
Proximity Hands		Doctor, chemist, etc. E.g., Ra, Na, P, I, As, C, S, Yt, Au	E.g., Ra, Na, I, As, Au
Surface contamination, especially hands	Generally assumed not effective on skin surface	Doctor, chemist, etc. Beta irradiation dominates gamma; E.g., Ra, P, Na, I, C, S, Sr, Yt, Au	
Inhalation	Everybody in the laboratories Lethal dose of alpha is small E.g., Ra, Rn, Pu, Po	Beta irradiation dominates gamma; some (e.g., rare earths) which are relatively less dangerous when ingested are yet fairly readily absorbed through the lungs	
Ingestion	Everybody; doctors and assistants most likely E.g., Ra, Rn, Pu, Po, etc., even though poorly absorbed	Contaminated wastes may spread hazard far and wide E.g., P, Na, I, C, S, Sr	
Parenteral absorption, wounds, etc.	Doctor and assistants E.g., Pu	Doctor and assistants But unimportant compared to surface contamination	
Percutaneous absorption	Doctor, chemist, etc. Any radioactive isotope in fatty base or in fat solvent		
Bad clinical judgment	Patients and experimental subjects a. By overdosing, total body dose; e.g., P, Na b. Through failure to consider large total accumulation of injury due to isotope's long half-life; e.g., 4 yr. Fe, 4,000 yr. C, etc., and confusion of 8 day I with 12 hr. I c. By erroneous estimation of the concentration in a particular organ; e.g., I, Sr, P		

possible to apply them to clinical problems and therapeutic arts. Are we physicians going to be able—as a profession—to proceed at equal speed in learning the art of protecting our patients, ourselves, our associates and the communities we live in from the grave and insidious dangers of these very poisonous substances? This paper is intended to point out the dangers and to make some suggestions for avoiding them.

The accompanying table is offered as a graphic summary of the hazards that have been discussed.

INSPECTION OF TRAINING FACILITIES IN RADIOLOGY BY THE AMERICAN BOARD OF RADIOLOGY

Since the formation of the American Board of Radiology in 1934 its members and sponsors have realized that the standards of its examination could not be raised higher than the standards of training in radiology. Prior to 1941 there was a marked paucity of available residencies and during those years the primary effort was devoted to encouraging institutions to inaugurate residency training. In September, 1941, the American Board of Radiology ruled that

after January 1, 1945, no candidate would be admitted to examination who had not completed three years of residency training in an approved department of radiology. Unfortunately on December 7, 1941, we were precipitated into World War II and our plans made only three months earlier had to be abandoned.

Immediately after the war was over the Board of Radiology, along with all specialty boards, realized that there would be many young men returning from service demanding residency training, and in order to accommodate these young men, we entered into an agreement with the Council on Medical Education and Hospitals of the American Medical Association to make a cursory inspection of the applications submitted by any department of radiology and to give temporary approval for residency training until such time as the Board and the Council could review these programs.

The time has now come when we consider this emergency to be over and we must put our house in order by raising the standards of training in radiology. There are many of the older institutions which have been approved for a great many years whose personnel in the department of radiology has changed considerably. Therefore, it has now been deemed wise by the Board to review all our residency programs, including those already approved, both permanently and temporarily, as well as those applying for approval.

The Council on Medical Education and Hospitals of the American Medical Association has done an outstanding job in inspecting and evaluating the residency programs in all specialties and has cooperated harmoniously with the Boards. We, therefore, have no desire or intention of interfering with this fine work, but it has been decided, with the full approval of the Council, that the Board of Radiology will conduct its own inspection of all its residency programs. It is not our plan, however, to repeat this survey for many years, if at all.

Between forty and fifty outstanding radiologists with teaching experience have been invited to assist in making the inspection. Each department of radiology offering training in radiology and which is either already approved or seeking approval will be visited by one of these men.

This program will require several months to complete and it is therefore hoped that those departments of radiology seeking initial approval will be patient with us until it is completed.

B. R. Kirklin, M.D., *Secretary*
American Board of Radiology

AVAILABILITY OF RADIOISOTOPES FREE OF PRODUCTION COSTS FOR CANCER RESEARCH

The Atomic Energy Commission announces that all radioactive material normally available under its isotope distribution program will be distributed, free of production costs, to qualified users of these materials in cancer research.

This represents a second step in the policy of the Atomic Energy Commission to make available increasing quantities of radioactive materials for cancer research. It may be recalled that on April 1, 1948, the Atomic Energy Commission made available, free of production costs, radioactive phosphorus (P 32), radioactive iodine (I 131), and radioactive sodium (Na 24) for use in therapy, diagnosis, and research in cancer and allied diseases.

Under this enlarged program radioactive materials will be allocated for use in (1) cancer investigations involving animal subjects, (2) research programs studying basic cellular metabolism of cancerous cells, and (3) experimental programs designed to evaluate therapeutic use of radioactive materials.

Applicants for materials must fulfill the requirements of the Atomic Energy Commission for users of radioactive materials and must offer assurance that there will be no resale or charges to patients for the isotopes procured under this program. Applications should be submitted on Form AEC 313, "Application for Radioisotope Procurement." To qualify under this program a

statement of the research nature of the project should be fully completed and attached to Form 313.

It is expected that most applications for use in human subjects will arise from institutions having a definite research program in this field. Applicants are not eligible to receive radioactive materials to be used in routine or nonexperimental programs for the treatment of cancerous or allied diseases, with the exceptions of P 32, I 131 and Na24.

All applications for radioactive materials for use in human subjects must be approved by the Subcommittee on Human Applications of the Commission's Committee on Isotope Distribution. The Subcommittee has established the following criteria for the allocation of radioactive materials for human use:

1. The physician using radioactive materials must be associated with a medical institution, hospital or clinic or other medical organization possessing adequate facilities for the proper use of such materials.
2. The use of these materials in human subjects must meet with the approval of a local isotope committee of the hospital or medical institution with which the physician is associated.
3. All clinical users of radioactive materials must be physicians in good standing with their local medical society and must have had previous clinical experience with radiation or radioactive materials or be directly collaborating with individuals possessing such experience.

More complete information relative to procurement of radioisotopes for use in human subjects may be found in "Radioisotopes for Use in Medicine," Isotopes Division Circular D-4.

Although radioactive materials distributed under this program will be free of production charges, a handling charge of $10 will be made on each shipment to cover the cost of packaging, monitoring, accounting and billing. Transportation charges will be paid by the applicant.

Applicants who procure processed radioisotope materials or compounds from other than Commission facilities may by agreement with the processor make application for replacement of the amount of activity delivered. The Isotopes Division will authorize replacement of all activity involved in the processing in the case of radioisotopes with half-life of less than thirty days. In no case, however, will replacement be considered if the value of the radioisotope in the delivered material is less than $10.

Authorizations which have been issued to this date may be amended to permit the applicant to receive the balance of the undelivered materials free of production charge, provided: (1) the applicant submits a written request for such amendment, (2) the request is accompanied by a complete statement of the research project, (3) the request is received prior to May 1, 1949, and (4) shipment has not been made by the supplier under the original authorization.

Isotopes Division Circular E-35
Oak Ridge, Tennessee

PRIVATE LIBRARY OF DR. GRUBBE GIVEN TO THE JOHN CRERAR LIBRARY

Dr. Emil H. Grubbe, pioneer in roentgen therapy, has given his private library to The John Crerar Library, according to an announcement just issued by Herman H. Henkle, the Librarian. The gift makes important additions to the research collection of the Library in the fields of the roentgen ray, roentgen therapy and related technical subjects. The collection given by Dr. Grubbe numbers about 1,000 volumes.

As an experimenter and manufacturer of roentgenologic apparatus, Dr. Grubbe first suffered roentgen-ray burns more than fifty years ago. On January 27, 1896, he exhibited the detrimental effects produced by over-exposure to roentgen rays to a group of physicians in Chicago. Acting on the suggestion that the new roentgen rays might have value in the treatment of diseased tissues, Dr. Grubbe applied roentgen rays to a number of patients. These experiments marked the beginning of roentgen therapy.

Five early roentgen-ray tubes used by Dr. Grubbe, original documents, letters, records and other evidence pertaining to Dr. Grubbe's claim to priority as the originator of roentgen therapy are on deposit with the Smithsonian Institution of the United States National Museum in Washington, D. C.

INSTRUCTION COURSES AT CINCINNATI MEETING

The Executive Council of the American Roentgen Ray Society instructed the President Elect to take a mail ballot of the membership regarding the question of having Instruction Courses at the next meeting of the Society in Cincinnati, October 4–7, 1949. Four hundred replies were received by February 15, 1949. Of these, 80 per cent were in favor, 17 per cent not in favor, and 3 per cent noncommittal. Accordingly, Instruction Courses will be given from 8:30 to 10:00 A.M. each day of the meeting under the direction of Dr. Harry M. Weber.

U. V. Portmann

ERRATA

In the article by D. Findlay and C. P. Leblond entitled "Partial Destruction of Rat Thyroid by Large Doses of Radioiodine," which appeared in this Journal, March, 1948, *59*, 387–395, the following corrections should be made:

On page 387, first column, line 7 of text, instead of " . . . mixture of $I^{131}+I^{131}$ . . . "

Read " . . . mixture of $I^{130}+I^{131}$. . . "

On page 387, first column, line 25 of the text, instead of " . . . in the form of I^{131} and I^{131}. . . "

Read " . . . in the form of I^{130} and I^{131}. . . "

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

Department Editor: GEORGE M. WYATT, M.D., 1835 Eye St., N.W., Washington 6, D. C.

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ROENTGEN DIAGNOSIS

NECK AND CHEST

BROUSTET, P. Sur un procédé simple pour apprécier la mobilité du coeur. (On a simple procedure for the evaluation of the mobility of the heart.) *Arch. d. mal. du coeur,* March-April, 1948, No. 3–4, pp. 169–174.

The author reviews briefly the orthodiagram method (of Vaquez and Bordet) of computing the mobility of the heart. Then he gives his modification of the method which consists in measuring the distances from the two borders of the heart to the left and to the right walls of the chest in the following fixed positions (the shoulders and the hips of the patient touching the screen firmly): vertical, patient inclined 50° to the left and lastly 50° to the right. Comparison of these distances gives an accurate measurement of the mobility of the heart. Normal and hypertrophic hearts have a good mobility (10 to 20 mm.). Fixity is pronounced in pleuropericardial adhesions of various causes. Also, fibrous tuberculosis, asthma and deformity of the chest wall are mentioned as causes of fixity of heart.—*J. N. Sarian, M.D.*

Fischmann, E. J., and Gwynne, F. J. The heart in rheumatoid arthritis. *Brit. Heart J.*, April, 1948, *10*, 125–134.

Recent reports suggesting the presence of cardiac lesions in a high proportion of patients with rheumatoid arthritis appear to be in conflict with clinical experience. In view of the scarcity of comprehensive clinical and the absence of roentgen studies of the heart in rheumatoid arthritis, and also the contradiction between clinical and pathological findings, there seems to be a need of further clinical and roentgenological material.

The series of patients studied consists of 60 selected from among patients with rheumatoid arthritis, eliminating those who are not typical or those who do not or cannot be satisfactorily studied in every particular.

The results of the investigation suggest the presence of roentgenologically evident, mainly left ventricular, cardiac enlargement in 23 per cent of patients with rheumatoid arthritis. On the other hand, it appears that the cardiac abnormality underlying the enlargement is characterized by the absence of recognized clinical and electrocardiographic manifestations of heart disease.

The 60 rheumatoid arthritic patients in this selected series were found to have normal blood pressure, no history of rheumatic fever, and no chest deformity, and to be able to stand upright for cardiac roentgenography. Clinical and electrocardiographic findings were negative apart from a tendency to low voltage of the standard leads. Roentgen examinations suggested the presence of cardiac enlargement in 23 per cent of patients. Enlargement of the left ventricle in 50 per cent of these, left ventricular and left auricular in 21 per cent, generalized in 29 per cent, and right sided in none of the hearts adjudged enlarged. The esophagus was displaced backward at the level of the left auricle in 29 per cent of the enlarged hearts.

It is thought probable that roentgenologically manifest cardiac enlargement in rheumatoid arthritis is an expression either of chronic rheumatoid carditis or a form of cardiac involvement due to the etiological factor of rheumatoid arthritis.

An attempt is made to explain the prevalence of the enlarged ventricle in cardiac enlargement and also the absence of clinical and electrocardiographic manifestations of heart disease in the presence of roentgenologically demonstrated enlargement.—*H. G. Reineke, M.D.*

Vaccarezza, Raul F., Lanari, Alfredo, and Soubrié, Alberto. Discrepancies between clinical-radiological and bronchospirometric findings. *Am. Rev. Tuberc.*, Feb., 1947, *55*, 128–143.

Fifteen cases were selected from a group of over 400 bronchospirometries in order to point out the discrepancies between clinical roentgenological and bronchospirometric examinations. The authors have attempted to differentiate the various factors responsible for these apparently paradoxical results, grouping them under four separate headings according to whether they arise in the lungs, bronchi, pleura, or chest wall.

1. Pulmonary Factors: Parenchymatous lesions may pass unobserved in the routine clinical-roentgenological examination, either because they are too small to be diagnosed by these methods, or because they are erroneously underestimated, as in the case of emphysema and diffuse fibrosis, or because their situation is such that they remain completely hidden. The latter is most likely to occur when dealing with the left lower lobe.

2. Bronchial Factors: Bronchial lesions may greatly interfere with ventilation, at times completely annulling the respiratory function of the entire lung, without any traces of this functional impairment being indicated in the ordinary roentgenogram.

3. Pleural Factors: Pleural lesions, mainly symphysis, hardening and thickening of the pleura, frequently diminish the functional value of the corresponding lung. In most cases, the oxygen consumption is particularly influenced, perhaps because of a pulmonary sclerosis of pleural origin. These lesions which are not always apparent in the roentgenogram, are frequently encountered, not only accompanying pulmonary lesions, but also in the course of an artificial pneumothorax.

4. Changes in the Chest Wall: The existence of painful phenomena, muscular atrophy, paresis or paralysis of the phrenic nerve may reduce the efficiency of the respiratory muscles on one side of the thorax.—*J. J. McCort, M.D.*

ABDOMEN

Holt, John F., Lyons, Richard H., Neligh, Rosalie B., Moe, Gordon K., and Hodges, Fred J. X-ray signs of altered alimentary function following autonomic blockade with tetraethylammonium. *Radiology*, November, 1947, *49*, 603–610.

Tetraethylammonium has the unique prop-

erty of blocking the transmission of impulses through the sympathetic and parasympathetic ganglia. The authors used the drug in examining its effect on the various portions of the alimentary canal. No effect was noted in the case of the esophagus either in normal cases or in cases of cardiospasm. In the stomach there was a prompt diminution of muscular tone and generalized dilatation. Peristaltic waves stopped almost completely, no appreciable barium leaving the stomach. Intravenous and intramuscular injections yielded the same results, except that the latter produced more prolonged effects. In the case of the small intestine, there was a profound inhibition of the propulsive movements; motility appeared to stop completely. The usual undulating pendulum movements also were not detected. In some cases, the pattern of the mucous membrane folds was unchanged for a prolonged period. Slight general dilatation was usually evident. All of the roentgenologic features however of a well-defined "deficiency pattern" as noted in various nutritional disorders, gastrointestinal allergy, diabetic neuropathy, etc., were not produced in most cases. Atropin and adrenalin in contradistinction to tetraethylammonium do not affect the regular movements of the mucosa, but do produce a decrease of the intestinal motility to a lesser extent. In the colon, the chemical caused no appreciable change in the haustral markings. Changes in motility were not demonstrated. However, while the drug was active, the colon could be considerably distended without producing a desire to defecate. It is possible that further study may give the drug a place in medical treatment although its use at present is very limited. In the meantime, it should be of definite value in the investigation of the normal and pathologic autonomic nervous system.—*J. Paul Bennett, M.D.*

POLLARD, H. MARVIN, BLOCK, MALCOLM, BACHRACH, WILLIAM H., and MASON, JOYCE. Treatment of peptic ulcer with enterogastrone. *Arch. Surg.*, March, 1948, *56*, 372–385.

A preliminary report of the authors' clinical and laboratory observations on the use of enterogastrone in the treatment of peptic ulcer, as well as its physiologic action in man, is given.

Twelve patients were given orally 8–16 grams of the drug per day for varying periods up to eleven months. Ten were relieved of symptoms but 2 had a recurrence of typical ulcer symptoms, having been treated six and ten months respectively.

Three of 16 patients given 200 mg. of enterogastrone intramuscularly had recurrences or no relief of symptoms. Daily dosage was twice the amount necessary to prevent ulcer formation in 79 per cent of Man-Williamson dogs.

Roentgenographic studies of 17 of the 28 cases after therapy showed improvement in 6 cases, unchanged in 8 and worse in 3 cases, a duodenal ulceration appearing during treatment.

Single intramuscular injections of 200–800 mg. of enterogastrone in persons with peptic ulcer, and daily oral or parenteral injections for periods up to eleven months, had no effect on the volume of fasting gastric secretion, volume of hydrochloric acid, pepsin concentration or type of response to a caffeine test meal.

The authors feel that their clinical data are inadequate for the establishment of any general conclusions concerning the efficacy of the drug in preventing or decreasing the incidence of recurrence of peptic ulcer because their period of observation is too short, and the dosage possibly too small. Inefficacy of the particular preparation or selection of inappropriate types of cases may also be a factor.

They do feel, however, that if the drug does have any beneficial effect it is through some mechanism other than altered gastric motility or secretion and that other methods of study must be used to follow possible beneficial effects. Larger doses of a more purified drug might help these cases.—*T. L. Martin, M.D.*

GRAHAM, RUTH, ULFELDER, HOWARD, and GREEN, THOMAS H. The cytologic method as an aid in the diagnosis of gastric carcinoma. *Surg. Gynec., & Obst.*, March, 1948, *86*, 257–259.

Carcinoma of the stomach is encountered more frequently than is any other malignant lesion today. Surgical extirpation has been the only effective means of treatment but the disease is so insidious in its onset that extirpation is rarely possible. Cancer of the stomach is usually moderately advanced before it produces any symptoms at all. If any significant increase in the rate of operability with expectation of cure is to be achieved some means of detecting the disease in its presymptomatic state must be devised.

In this paper the authors present a preliminary report on their experience with a diag-

nostic measure which may be of value in discovering early gastric carcinoma—cytologic examination of gastric fluid for the presence of malignant cells.

Summary

1. The cytologic method of diagnosis has been applied to gastric aspiration in 50 patients with gastric symptoms.

2. A description is presented of the normal and malignant cells which are noted in gastric fluid.

3. Of 24 patients proved to have carcinoma of the stomach, smears were positive in 15 instances.

4. Of 7 patients with resectable lesions of the stomach, smears proved to be positive in 5 cases.

5. Of 26 patients without cancer the smear was reported positive in 1, a man with a benign gastric ulcer.

6. Two patients had extremely early malignant lesions. In both, the lesions were detected by the cytologic technique.—*Mary Frances Vastine, M.D.*

Hodges, Fred J., Rundles, R. Wayne, and Hanelin, Joseph. Roentgenologic study of the small intestine. II. Dysfunction associated with neurologic disease. *Radiology*, December, 1947, *49*, 659–674.

The authors present cases to show that gastrointestinal symptoms are produced by some neurologic diseases which affect the autonomic nerves. Roentgen studies have demonstrated abnormal intestinal function in these patients.

Small intestinal studies were done on selected patients with neurologic disease which included 35 cases of diabetic neuropathy, 20 cases of pernicious anemia, 5 cases of tabes dorsalis, 7 cases of miscellaneous neurologic disease, and 8 cases with sympathectomy.

The chronic neuropathy which results from diabetes shows predilection for the autonomic nerves as evidenced by sweating deficiencies, neurogenic bladder paralysis, etc. Over 60 per cent of the patients with diabetic neuropathy developed gastrointestinal symptoms, i.e. chronic constipation, diarrhea, cramps, nausea and vomiting. The principal roentgenographic observations were delayed gastric emptying, prolonged transit time through the intestines, and segmentation of the barium column.

Of 20 patients with a severe pernicious anemia 10 had developed neurologic disorders but only 5 of these showed intestinal abnormalities similar to those in the group with diabetic neuropathy. The remainder of the group showed no appreciable evidence of intestinal dysfunction. No untoward disturbance of intestinal physiology was noted in patients with tabes dorsalis even though 3 of the 5 had "gastric crises" and another had marked gastrointestinal symptoms. Intestinal abnormalities were observed in a case of lead poisoning and also in a patient with autonomic nerve paralysis following an acute infection.

The rather minor role of extrinsic sympathetic innervation of the gut as compared to the greater importance of the parasympathetic autonomic nerves is demonstrated by gastrointestinal studies on sympathectomized patients (for arterial hypertension) and on patients with vagotomy (for peptic ulcer) respectively. The latter group showed both motor and secretory dysfunction of the intestines which resembles the changes described in diabetic neuropathy. The sympathectomized patients developed gastrointestinal symptoms following operation but this subsided in a few weeks.

It is pointed out that while intestinal dysfunction may occur in the presence of organic disease a great variety of conditions namely, nutritional disease, intestinal parasitism, hypoproteinemia, autonomic nerve disease, neuromuscular degeneration, purpura, etc., may produce the same findings.—*George P. Keefer, M.D.*

McGuff, Paul. Dockerty, Malcolm B., Waugh, John M., and Randall, Lawrence M. Endometriosis as a cause of intestinal obstruction. *Surg., Gynec. & Obst.*, March, 1948, *86*, 273–288.

An analytic study of clinical data on 16 from the current series of cases of intestinal obstruction caused by endometriosis has been presented as well as the results of a pathologic study of these cases.

1. To make the diagnosis of endometriosis as a cause of intestinal obstruction the possibility of its occurrence should be kept in mind in every case of intestinal obstruction in which the patient is a woman from thirty to fifty years of age.

2. Acquired dysmenorrhea, menstrual periodicity of symptoms, sterility, rectal or pelvic pain, absence of loss of weight, the presence of associated uterine fibroids or ovarian cysts and

a long history of intestinal symptoms which suggest progressive intestinal obstruction with frequent exacerbations at menstruation are most important points in the diagnosis of this condition.

3. Gross blood in the stool is infrequent. If present at the time of menstruation it is of significance.

4. The symptoms of menorrhagia and metrorrhagia are not the symptoms of endometriosis per se but rather the symptoms of associated pelvic pathologic lesions.

5. When the lesion is in the lower bowel the sigmoidoscopic examination may show an intact puckered mucosa in the presence of an extrarectal mass. On the roentgenogram, a long inconstant filling defect with sharp regular borders and an intact mucosa will be noted in these cases.

6. Obstruction of the ileum as caused by endometriosis presents a less characteristic clinical picture than that in the sigmoid or below. The mechanism of ileal obstruction was usually due to kinking caused by the endometriosis while the obstruction in the sigmoid and below was more often due to an impingement of the endometrioma into the intestinal lumen.

7. Microscopically, endometrial glands and stroma were found in all layers of the intestinal wall. They seemed to be most diffusely dispersed in the muscular layers. The endometriomas of the sigmoid were of the discrete or deep type while the endometriomas of the ileum were located closer to the serosa.

8. A plea is made for biopsy, frozen section and pathologic confirmation of the clinical diagnosis in all cases of endometrioma obstructing the bowel as carcinoma can be positively excluded only by this method.—*Mary Frances Vastine, M.D.*

SPENCER, JACK, and THAXTER, LANGDON T. Acute obstruction of the small bowel. *Radiology*, November, 1947, *49*, 611–619.

The authors have obtained the material for their paper from the records of the Maine General Hospital where for years a scout film of the abdomen was taken in all undiagnosed acute abdominal cases, especially when obstruction was suspected. They emphasize the value of the roentgen findings in small intestinal obstruction, these to be taken in conjunction with the history, physical findings and laboratory results. Gas in the small intestine—except in young children—is abnormal. It is noted in reflex ileus as well as in mechanical; in the latter, there is not only gas but dilatation. Occasionally in colon obstruction, gas is noted also in the small intestine. The site of the obstruction can be localized by (1) the location of the gas and (2) characteristics of the mucosal folds in the different levels of the intestines. Gas in the jejunum is mostly in the left upper abdomen; while that in the ileum is mostly in the right lower. The jejunum has the transverse mucosal folds close together giving the "herring-bone" appearance; while the ileum has the folds farther and farther apart as one progresses downward. The location of the colon and its characteristic haustral markings aid in identifying gas therein.

One hundred cases of small bowel obstruction which had both roentgen studies and surgical confirmation are analyzed. A summary is given indicating the etiological factors of the obstruction in the cases discussed. The most common cause was adhesions, with or without previous laparotomy (78 per cent). Other causes were internal hernia, Meckel's diverticulum, gallstones, intussusception and ileitis. The roentgen findings were conclusive of obstruction in 94 per cent of the cases. In 50 cases, when the site of the obstruction was indicated in the operative notes, this was found to correspond with the roentgen findings. In 33 cases, the obstruction was in the terminal ileum; in 9 cases, in the mid small bowel; and in 6, in the jejunum. Barium enema was resorted to in 8 cases to localize the gas.—*J. Paul Bennett, M.D.*

OSGOOD, ELLIS C. The role of the radiologist in the management of patients with intestinal obstruction, with special reference to the use of the Miller-Abbott tube. *Radiology*, November, 1947, *49*, 529–555.

The author evaluates the role of the roentgen examination in the management of patients with intestinal obstruction. He points out that the roentgenologist's opportunity in this field has been extended recently by the introduction and use of the Miller-Abbott tube.

While the clinical diagnosis of intestinal obstruction is often adequate, the roentgen examination offers valuable confirmatory evidence and often it is useful in locating the obstruction. Supine and erect anteroposterior films of the abdomen should be taken initially. The earliest finding in small intestinal obstruction is a small

segment of distended intestine, clean-cut in outline, often resembling a hairpin. Initially it may contain no fluid level, but as the obstruction persists, later examination will show fluid levels and the coils will increase in size and number to produce the "stepladder" pattern. In the earlier stages it is possible to distinguish, by its delicate transverse striations, the jejunum from the ileum but when the dilatation becomes marked the appearance of all levels of the small intestine becomes quite similar. Usually the colon occupies the peripheral portions of the abdomen and the haustral markings can be identified. However, these are not seen in the lower descending colon and sigmoid, and distention of this portion may very closely resemble distended loops of ileum.

When the colon is obstructed there is usually distention of the segments proximal to the site of the obstruction. Distended loops of small intestine may or may not be present. The cecum is usually the site of the greatest distention, even though the obstruction may be in the descending colon or sigmoid.

In reflex ileus, both the small and large intestine are usually involved. The distention is less likely to be uniform so that loops of both small and large intestine are irregularly outlined and there is a conspicuous absence of a pattern suggesting continuity, which is the rule in organic obstruction. Not infrequently a mechanical and reflex ileus may coexist.

When there is distention due to intestinal obstruction the Miller-Abbott tube allows suction to be applied at, or just proximal to the obstruction. This has been shown to be more effective than duodenal suction drainage. The point of arrest in the passage of such a tube may localize the site of obstruction, particularly if barium is injected through the tube after it has been arrested. As the bowel proximal to the suction is decompressed by suction, peristalsis returns and a normal segment of bowel is then available for the introduction of liquid nutriments. It is possible for the surgeon to prepare the patient for operation and this converts an emergency into an elective procedure. In cases of reflex ileus it is a therapeutic end in itself, and the results have been brilliant. The prophylactic introduction of the tube before surgical procedures involving resection of the large intestine has also proved very valuable.

The Miller-Abbott tube should not be used in cases of strangulation or gangrene of the intestine if operation is thus delayed, but it may be useful postoperatively. It should not be used in large intestinal obstruction, except in those cases where there is reflux distention of the small intestine. In such cases it may be introduced when the patient is being prepared for operation.

Complications are few but they include irritation of the upper respiratory passages, laryngeal damage and injury to esophageal varices. There have also been complications resulting from excessive coiling of the tube and from inability to deflate the balloon.

The author describes the technique of the passage and care of the Miller-Abbott tube in considerable detail. He rightly points out the value of experience, persistence, patience and the use of flouroscopic control. The injection of 2 to 3 cc. of mercury into the balloon has been a very effective aid in the passage of the tube through the pylorus. In cases of simple mechanical obstruction, the tip of the tube usually moves quite rapidly and may be in the terminal ileum in twelve to thirty-six hours, if the obstruction is not higher. In paralytic obstruction the progress is much slower. When the tube is withdrawn, this should be done slowly, over a period of several hours.

After the tip of the tube becomes arrested at the point of the obstruction, it is not difficult to inject barium. This should be rather dilute—one part of barium to four parts of water. This will often show that the obstruction is incomplete, although clinically it may seem complete. The segment of intestine beyond the point of obstruction should be of normal caliber. If this is not the case, the possibility of a more distal obstruction should be considered and observation continued for a longer period of time. The main value of injection of barium lies in the determination of the presence or absence of obstruction. The nature of the obstruction is not always revealed, although sharp angulation with incomplete obstruction is suggestive of adhesions. The demonstration of the anatomical degree of obstruction does not always determine whether or not eventual operation will be required.

In the past forty years there has been a significant drop in the mortality rate for patients with intestinal obstruction. Earlier recognition, due in great part to more frequent roentgen examination and greater experience with roentgen findings has certainly contributed to this decline. Improved operative technique, the newer concepts of pathologic physiology and

the use of sulfonamides have also helped. It is difficult to assess the exact contribution of the Miller-Abbott tube as compared with the simpler and older method of duodenal suction in this reduced mortality. However, various publications seem to show that the Miller-Abbott tube has resulted in a statistically significant reduction of mortality.

The part the roentgenologist may play will vary from simple flouroscopy to more or less complete responsibility for the passage of the tube and its care. In highly organized clinics, a system of division of labor will probably prevail, but it is essential that someone assume definite responsibility for its use. Only under such circumstances can the procedure be successful in a high percentage of cases.—*Arthur E. Childe, M.D.*

Doub, Howard P. Malignant tumors of the small intestine. *Radiology*, October, 1947, *49*, 441–451.

The paper is based upon a series of 52 malignant tumors of the small intestine. Emphasis is placed upon detailed serial studies of the small intestine for accurate localization and differentiation of these lesions.

The duodenal lesions represented 44 per cent of the series. There were 21 cases of primary carcinoma and 1 case of lymphosarcoma in the duodenum. Of the duodenal tumors, 17 per cent were supra-ampullary, 61 per cent peri-ampullary and 22 per cent infra-ampullary. Right upper quadrant pain, weight loss, a palpable tumor mass and occult blood in the stools are frequent clinical findings. Gastric obstruction is frequent in supra-ampullary lesions, while jaundice is encountered in peri-ampullary lesions. The roentgen findings vary from minimal mucosal deformities to constricting lesions, filling defects or ulceration.

Similar symptoms and roentgen signs were encountered in jejunal and ileal tumors. Jejunal tumors constituted 27 per cent of the series and included 3 carcinomas, 3 lymphoblastomas, 1 case of leukemic infiltration, and 1 carcinoid tumor. In the ileum there were 4 carcinomas, 4 lymphoblastomas and 3 carcinoids, constituting 21 per cent of the total series. The clinical symptoms of this group are those of obstruction; either intussusception in the polypoid type, or gradually increasing obstruction in the constricting type. Clinically, weight loss, palpable tumor mass, secondary anemia and occult blood in the stools are frequent findings. The roentgen examination may reveal obstruction, filling defects, or more diffuse wall infiltration.

Five metastatic carcinomas were seen, representing 10 per cent of the series. Their clinical findings and roentgen appearance are not described.

Eight lymphosarcomas were encountered, 1 in the duodenum, 3 in the jejunum and 4 in the ileum. Lymphosarcomas rarely obstruct. Localized dilatation associated with some areas of narrowing and partial obstruction are the most characteristic findings.

Four carcinoid tumors were reported in the series, 1 in the jejunum and 3 in the ileum. Two of these were associated with definite defects and partial obstruction.

Clinical histories and roentgenograms are included.—*Gordon J. Culver, M.D.*

Wheeler, Digby. Diverticula of the foregut. *Radiology*, October, 1947, *49*, 476–482.

The author gives a brief discussion of the apparent confusion existing in the classification of diverticula, and suggests that the simple classification of Odgers, namely, primary and secondary, is the best.

This paper is based on the barium studies of 20,000 patients in which diverticula are considered in the following order: (*a*) esophageal-pharyngeal diverticula, (*b*) diverticula of the thoracic esophagus, (*c*) diverticula of the stomach, (*d*) duodenal diverticula. The incidence for each group is given. The author concludes that only the esophageal-pharyngeal diverticula cause symptoms, and that the remaining are usually only incidental findings.—*Gordon J. Culver, M.D.*

Zimmer, Johannes. Microcolon. *Acta radiol.*, 1948, *29*, 228–236.

The congenitally small colon or microcolon (meconium ileus) is a condition in which the entire large intestine (except the rectum) of a newborn infant is found to have a diameter of about 4 to 8 millimeters. Also, the following features are noted: (1) hypertrophy and dilatation of a segment of the small intestine—usually in the ileum (3–5 cm. in diameter); (2) a sudden or more gradual change of caliber in the small intestine distal to the dilated segment with narrowed lumen containing inspissated meconium; (3) no demonstrable stenosis or atresia of the gastrointestinal tract. This is called the primary type of microcolon since no

anatomical obstruction of the gastrointestinal tract is seen to account for its development. (4) If, however, a congenital obstruction proximal to the sigmoid colon is present, a microcolon has infrequently been found at operation or postmortem. Depending upon the site of the obstruction, whether proximal to or in the colon, the entire large intestine or part of it is reduced in size. This is called the secondary type of microcolon since the obstruction is the primary cause for the underdevelopment of the colon.

Conclusions. The primary type of microcolon (meconium ileus),

A. May be suspected if the following symptoms are present:
   1. No meconium passed by rectum after birth.
   2. Vomiting starts shortly after birth, being unrelated to meals, and the vomitus being bile-stained.
   3. No palpable atresia of the anus.

B. May be considered definite if the roentgenographic findings show:
   4. No fluid levels in the distended loops of the bowel.
   5. The distended loops contain coarse, granulated fecal matter (inspissated meconium).

In cases of atresia or stenosis (secondary type of microcolon) fluid levels may be seen roentgenologically. Granulated fecal matter is not seen.—*Mary Frances Vastine.*

GILCHRIST, R. K., and DAVID, VERNON C. Prognosis in carcinoma of the bowel. *Surg., Gynec. & Obst.*, March, 1948, *86*, 359–371.

In this study of 200 patients having resection for carcinoma of the colon, there was a 96.5 per cent five year follow-up. One hundred and fourteen were known to be alive five to ten years (57 per cent). In the study of the surgically removed specimens, microscopic sections were made of over 10,000 different lymph nodes, carefully plotted as to location to tumor and surgical landmarks. A number of facts stand out:

1. There is need for uniform and accurate description of the location of the tumor when discussing the value of different operative procedures in carcinoma of the colon and rectum.

2. Cases of palliative resections where known metastases are left in the liver, lung, etc., should not be included in discussions of surgery for cure of carcinoma.

3. The 37.5 per cent five year survival rate of those having carcinoma of the left side of the colon when lymph node metastases were present indicates the need for the widest possible resection of mesentery rather than the usual V-shaped wedge of mesentery resected in these cases. The favorable prognosis seen in right colon lesions having involved nodes is undoubtedly due to the wide resection of mesentery (54 nodes per specimen) performed when doing an ileotransverse colon resection and anastomosis.

4. Retrograde metastases to nodes 1 to 5 cm. below the tumor occurred in 7 of the 153 tumors below the promonotory of the sacrum (4.6 per cent).

5. New carcinomas developed in 7 patients who had had resections.

6. In view of the appreciable percentage who develop recurrence in the fourth and fifth year after operation, it seems unwise to consider anything less than a five year survival as a cure.

7. In carcinoma at and below the peritoneal reflection where lymph node metastases were present in the surgical specimens, 23.2 per cent developed local recurrences and 15.9 per cent developed liver recurrences within 5 days.

8. Postmortem examination of those dying in the hospital after resection for carcinoma of the rectum showed that the ordinary postmortem examination will usually fail to demonstrate small metastases in the remaining retroperitoneal lymph nodes.

This study indicates the need for the widest possible resection in carcinoma of the colon. Lesions which are partially or completely below the peritoneal reflection have a high incidence of local and liver recurrence. The Miles operation seems to give the best chance of cure here.

The real question in the discussion about end-to-end anastomosis should be "Can you remove all of the cancer?" and not, "Can you sew two ends of bowel together?" Obviously, in those intraperitoneal lesions below the promontory of the sacrum which are large or have palpably enlarged nodes, the abdominoperineal resection will give a greater chance of cure.—*Mary Frances Vastine, M.D.*

GAMBILL, EARL E., and PUGH, DAVID G. Pancreatic calcification. *Arch. Int. Med.*, March, 1948, *81*, 301–315.

By the term "pancreatic calcification" is meant calcareous deposits in the pancreas,

either within the ducts or in the parenchymatous tissue outside the ducts or in both. From a practical clinical standpoint the inclusive term "pancreatic calcification" seems preferable to the term "calculi." Accordingly, the authors have refrained from using the word "calculi" in order to avoid the possible implication that calcific deposits are necessarily located within the ducts.

The objectives of the present analysis were (1) to study the symptomatology and the roentgenologic features in cases of pancreatic calcification, and (2) to learn whether there is any correlation between the extent of calcification in the pancreas and the incidence of clinical manifestations, with particular reference to the manifestations of other complications of pancreatic disease such as diabetes mellitus and steatorrhea.

Evidence of pancreatic calcification is primarily a matter of roentgenologic diagnosis in the absence of surgical or postmortem examination of the pancreas since there are no symptoms or signs by which calcification can be diagnosed.

In a study of 39 cases of pancreatic calcification, selected solely on the basis of roentgenologic evidence of calcification, it was found that calcareous deposits in the pancreas were usually but not always associated with relapsing pancreatitis. Commonly the symptomatology was that of pancreatitis, although in approximately two-fifths of the cases there was either no history of pancreatitis or a doubtful one. Among cases in which a definite history of pancreatitis was obtained, calcification became evident in one-fifth in one year after the onset of pain, but in another fifth calcification was not discovered until after eleven to twenty-two years.

A diagnosis of relapsing pancreatitis is justifiable in the presence of recurrent severe attacks of pain in the upper part of the abdomen commonly lasting for hours or days and often requiring the administration of more than one hypodermic injection of opiate, provided other causes for such attacks have been excluded.

As might be anticipated, there seemed to be a high degree of positive correlation between the extent of calcification in the pancreas and the incidence of diabetes and steatorrhea. Thus in 23 cases in which the calcification was limited to the head of the pancreas only 4 instances of diabetes or steatorrhea occurred, whereas in 11 cases in which calcification involved the entire pancreas there were 9 instances of diabetes or steatorrhea. It should be emphasized, however, that extensive pancreatic calcification is not always associated with signs of pancreatic insufficiency.

There appeared to be no positive correlation between the size, shape or method of grouping of the calcareous deposits and the degree of pancreatic insufficiency. Moreover, the extent of calcification and the degree of disturbance of pancreatic function were not necessarily related to the length of time during which a patient had been suffering from the severe seizures of pain.

It is in the group with unsuspected disease that the diagnosis of calcification is most important, since such a diagnosis may direct attention to pancreatic disease that might otherwise remain unrecognized. Any roentgenograms that include all or part of the pancreatic region may reveal calcareous deposits. In this series the deposits were seen most frequently in cholecystograms or in localized roentgenograms of the gallbladder region.—*Eugene J. MacDonald, M.D.*

GYNECOLOGY AND OBSTETRICS

ARNESON, A. N. Clinical diagnosis of carcinoma of the cervix. *Radiology*, October, 1947, *49*, 400–402.

Biopsy is the basis for diagnosis of cancer of the cervix. The cases are grouped clinically into three main biologic groups which form some foundation for prognosis:

1. The everting or cauliflower types which grow rapidly, bleed early and are frequently limited to the cervix. They are radiosensitive and because of their early symptomatology present a favorable prognosis.

2. The infiltrating type growing slowly, bleeding late, with a maximum of fibroblastic activity and scant blood supply offers a poorer prognosis. This unfavorable outlook is due to resistance to irradiation and the fact that the disease is usually more advanced by the time symptoms appear.

3. Cratered lesions which may begin as one or the other of the above types. The degree of infection usually present may result in increased radioresistance and an extensive breakdown of tissue.

Prognosis can be more accurately established if biologic qualities are considered in conjunction with the stage of the clinical advance and histopathologic appearance of the biopsy specimen.

A plan of low intensity irradiation protracted over a long period is more effective in all three biologic types. The importance of a thin watery discharge is worthy of serious attention.—*J. Maxey Dell, Jr., M.D.*

Siebert, Walter J. Pathologic aspects of carcinoma of the cervix uteri. *Radiology*, October, 1947, *49*, 403.

Chronic cervicitis precedes cancer in approximately 75 per cent of cases. An average of 1 to 3 per cent of supravaginal hysterectomies, without removal of the cervix, are followed by cancer. Histopathologic grading is of value in prognosis. Single sections of the specimen have often proved negative in cases in which serial sections of the same lesions revealed early carcinoma.—*J. Maxey Dell, Jr., M.D.*

Brewer, John I. Carcinoma of the cervix; surgical aspects. *Radiology*, October, 1947, *49*, 404–405.

Surgery should be limited to Stage I or II patients, under fifty, in good physical condition, with no contraindication to operation. Also the patient must be thin (and this is most important). A general swing toward surgery for carcinoma of the cervix should not be made at this time. Surgery should be used only as an adjunct to irradiation.—*J. Maxey Dell, Jr., M.D.*

Heckel, George P. The syndrome of ovarian pain and insufficiency; importance of conserving ovarian tissue. *Surg., Gynec. & Obst.*, March, 1948, *86*, 260–272.

The author summarizes and makes his conclusions as follows:

1. Ovarian pain can occur in the absence of any demonstrable lesion of the ovary and it may have no regular relation to the menstrual cycle. Its frequent association with menstrual irregularities indicates that the pain is itself a sign of ovarian dysfunction.

2. This syndrome of ovarian pain, menstrual aberrations, and other signs of ovarian failure such as hot flashes, occurs in all ages of reproductive life.

3. The more frequent occurrence of pain on the right side in these cases in addition to other evidence suggests that the right ovary in woman is the more active.

4. By the presentation of cases in which ovarian tissue has been removed, in women and the citing of the known effects of partial castration in animals, the importance of an adequate mass of ovarian tissue for normal function is shown, and the need for conserving ovarian tissue in women is stressed. If one ovary is removed because of this type of pain, signs of ovarian insufficiency and pain in the remaining ovary may be expected.

5. The beneficial effect of therapy with estrogen including alleviation of cyclic intermenstrual pain without the prevention of ovulation suggests that the importance of the mass of ovarian tissue lies in its production of estrogen.

6. A theory of ovarian function is presented which includes the role of the uterus.—*Mary Frances Vastine, M.D.*

NERVOUS SYSTEM

Camp, John D. Symmetrical calcification of the cerebral basal ganglia. *Radiology*, November, 1947, *49*, 568–577.

Twelve cases have been observed by the author in which there were symmetric calcification in the basal ganglia and definite clinical evidence of parathyroid insufficiency and tetany. In one, this calcification followed a thyroidectomy at the age of nineteen years but in the other 11 the disease was the spontaneous type. The pathologic basis for the roentgenologic changes is a colloid deposition in and around the finer cerebral blood vessels, with subsequent calcification of the deposits, which coalesce and form vascular sheaths and concretions. The capillaries may be occluded but the lumens of the arteries are rarely narrowed.

The symptoms in general include the various complications of chronic parathyroid insufficiency, namely, cataracts, convulsions, mental retardation, and trophic changes. In none of the 12 cases did an "attack" occur after the institution of treatment for parathyroid insufficiency, and mental improvement was marked, indicating the importance of searching for parathyroid insufficiency in the presence of roentgenographic evidence of symmetrical calcification of the cerebral basal ganglia.

The roentgen appearance is distinctive, although the degree and extent vary considerably. In early stages there are small, irregular, discrete, symmetrically distributed shadows of increased density in the region of the various basal ganglia, especially the putamen and caudate nucleus. When more marked the shadows become denser. Calcification in the dentate nucleus of the cerebellum takes on a wavy, linear appearance and similar calcification may occur in the folds of the cerebellar hemispheres.

Calcification may also appear in the deeper layers of the cerebral cortex.

It is important and usually easy to differentiate this type of calcification from that due to a neoplasm and also from calcification in the choroid plexus of the lateral ventricle. It should also be differentiated from the types of calcification which occur in tuberous sclerosis and in toxoplasmosis. Occasionally symmetric calcification of the basal ganglia is encountered in patients who do not suffer from parathyroid insufficiency.—*Arthur E. Childe, M.D.*

TARLOV, I. M. Spinal extradural hemangioblastoma roentgenographically visualized with diodrast at operation and successfully removed. *Radiology*, December, 1947, *49*, 717–723.

The author defines hemangioblastoma as a true neoplasm composed of growing angioblasts and differentiates it from hemangiomas which are vascular malformations. An interesting case report is given which brings out all of the classic picture of a lesion of the spinal canal producing pressure on the spinal cord and eroding the pedicles of the vertebrae.

Treatment of the patient by laminectomy alone was unsuccessful and on re-operation the vascular tumor mass was exposed and portable roentgenograms made after the injection of diodrast into the tumor clearly defined the lesion and revealed a large blood vessel at its upper pole.

The author cites the use of diodrast injection at the operating table as a unique experience and one which made the successful removal of the tumor possible. He concludes that this technique may prove useful to others in outlining the limits of certain vascular lesions.—*Richard E. Kinzer, M.D.*

WELCH, C. S., ETTINGER, A., and HECHT, P. L. Recklinghausen's neurofibromatosis associated with intrathoracic meningocele. *New England J. Med.*, April 29, 1948, *238*, 622–625.

The association of anterior intrathoracic meningocele with neurofibromatosis is not generally recognized. In a patient with neurofibromatosis, discovery of a paraspinal mass usually suggests a provisional diagnosis of neurofibroma. However, 3 of the reported 4 cases of anterior intrathoracic meningocele occurred in patients with neurofibromatosis.

Films of the authors' patient, a woman of forty-one with known neurofibromatosis, showed a rounded left paravertebral mass, with widening of the sixth intercostal space and a kyphoscoliosis convex to the left at this level. The ribs, vertebral bodies, and transverse processes adjacent to the mass were eroded. Thorocotomy revealed a meningocele presenting through an enlarged sixth intervertebral foramen.

The authors suggest that paravertebral neurofibroma is uncommon in patients with neurofibromatosis, and that anterior meningocele may occur in these patients with comparable frequency. Differential diagnosis between the two lesions is important, since unwary surgical attack may result in fatality. The meningocele is apt to lie near the apex of a kyphoscoliosis, and may erode bone, but does not induce cord compression. Lipiodol myelography may be diagnostic if the opaque oil can be introduced into the meningocele sac.—*Henry P. Brean, M.D.*

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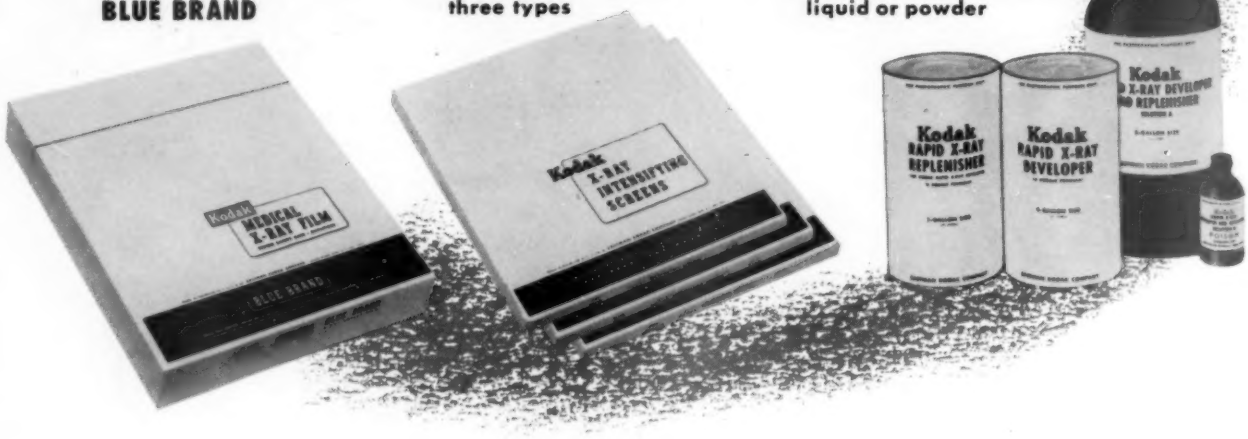

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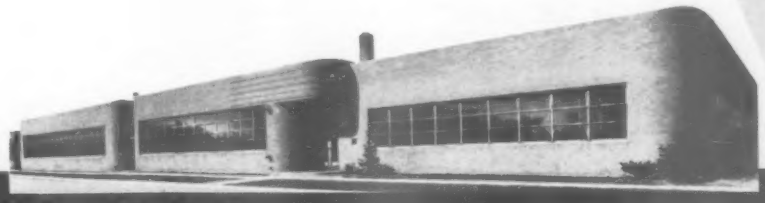

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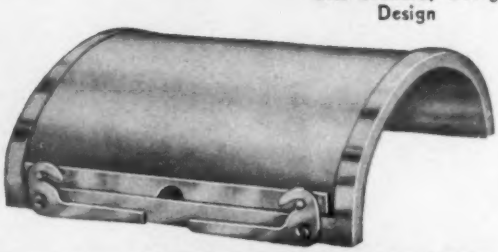

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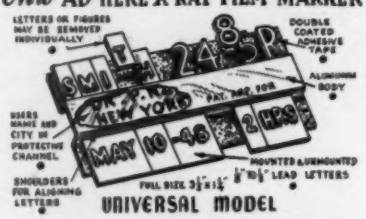
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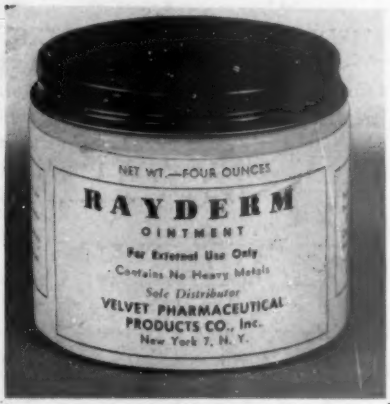

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